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BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 2 1947

THE PART OF CHEMISTRY IN THE NEW THERAPEUTICS*

BY

Sir HENRY DALE, O.M., G.B.E., F.R.C.P., F.R.S.

The relations between Chemistry and Medicine have varied very widely over the centuries. In origin they were more closely related than some others of the major departments into which science has become differentiated, but I shall not discuss the more precise nature of their original connexion—whether chemistry arose from attempts to explore the therapeutic aspect of medicine, or whether chemistry and medicine began together to grow out of the teaching and experiments of the alchemists. It is of interest, I think, to note that chemistry and the physiological basis of medical knowledge seem to have acquired a common interest at some of the great formative periods in the history of experimental science—with the advances made by Boyle, Hooke, Mayow, and their group towards the end of the seventeenth century, and again with those due to Priestley and Lavoisier a century later, from which we are accustomed to date the rise of modern chemistry.

Organic Chemistry in Medicine

In the earlier part of the nineteenth century organic chemistry became differentiated as the chemistry of the products characteristic of the tissues and the activities of living organisms. Then the success of chemists in reproducing some of these, and imitating others, by artificial synthesis attracted organic chemistry for a period into exploring a vast new range of artificial compounds of carbon, to meet demands of industry and the arts as well as to extend knowledge and theory of the reactions and properties of such organic compounds and the scope and methods of practicable synthesis. A case could be made, I think, for suggesting that in the latter third of the nineteenth century medical science may have been retarded on that side of its development by default of the earlier linkage with chemistry. So far as the experimental disciplines of medicine were using chemical methods at that period, they were using them, in the main, at a relatively superficial level, so that men spoke in those days of "chemical physiology" and "chemical pathology." It might be suggested, on the other hand, that such delay represented a phase of preparation for later advance; that medical science was indeed engaged in necessary levelling, clearing, and tilling of the land, and that in the new century organic chemistry, with an immensely strengthened equipment, would the more rapidly make fresh and fertilizing contact with physiology and pathology, and that seed and soil would then alike be ready to produce the harvest of biochemistry and chemotherapy which we are even now reaping.

You will have in mind the recent loss from our British circle of scientific men and from that of the world's leaders in biochemistry of Frederick Gowland Hopkins, whose active years bridged the turn of the century. His earliest attempts and achievements show Hopkins to have possessed a natural genius for the methods and ideas of organic chemistry and a special interest for applying these to problems of biology and medicine. But Hopkins, I know, had in those earlier years the feeling that, whatever the precision and the significance of his results, since his work was done with a biological or medical approach and in a medical centre it would arouse no interest and obtain no recognition in the circles of official chemistry. One who preceded Hopkins as a pioneer of such true biochemistry in this country and in the world—J. W. Thudichum—had received little recognition as a chemist and even opposition and discredit from others using chemical methods in medical science, though many of his remarkable discoveries, made much in advance of their time, have in later years been rediscovered, confirmed, and reinstated. Hopkins was, happily, to live long into the era of recognition and honour for biochemistry and for himself as one of its pioneers and leaders, and to remain its active devotee till his recent death in the fullness of years.

Whatever the factors which may have contributed to the change, as we now approach this century's middle years and look back to its beginning we become aware of the astonishing range and rapidity with which a new community of interest and action has developed between chemistry on the one side and experimental medicine and biology on the other. First on its organic side, and then at the numerous growing-points on its margin with physics, we see chemistry acquiring relations of growing intimacy and deeper penetration with almost every active phase of advance in the physiology and pathology of animals and plants, and the accent becomes ever stronger on the chemistry in biochemistry. A speaker with suitable equipment could easily use the whole of the time at my disposal in expounding the transforming effects of this more intimate association with chemistry on any one of a large number of special aspects of biological or medical investigation—advances in structural knowledge of the different types of the organic components of the living substance, of the proteins, the carbohydrates, the fats, the lipins, the nucleotides and nucleic acids, of their metabolism, and of the specific differences and immunological reactions of some of them; of the range of characteristic end-products—alkaloids, purine derivatives, and the rest—of the metabolism of animals and plants; of systems of enzymes and

*A lecture delivered at the XIth International Chemical Congress, London, 1947.

coenzymes and their specific substrates; of vitamins and hormones. An attempt merely to complete such a catalogue would make too heavy a demand on my time and your endurance. I must choose one limited field of such co-operative action of chemistry with experimental medicine for more detailed discussion; and I propose to invite your special attention to some of the recent contributions which synthetic chemistry has made to the specific medicinal treatment of diseases, and in particular of diseases due to infections.

Search for Specific Remedies

It is of interest to recognize in retrospect that the very conception of a specific therapy of diseases, in the sense of a systematic search for remedies dealing with their causes, is of remarkably recent origin. Till the end of the nineteenth century was becoming near it was almost a matter of assumption that the function of medicinal treatment was to relieve symptoms, and that the removal of the cause of a disease must be left to nature. Then began the recognition that certain diseases were due to defects of natural hormones, and, later, that others were due to the lack of vitamins in the food. Such are not here my special subject, and in passing we can only note the revolutionary contribution which, by the identification and synthesis of these substances largely in the short interval between the two world wars, chemistry, in alliance with experimental medicine, has made to the specific prevention and treatment of such diseases of deficiency. The first world war was nearing its end before the hormone of the first deficiency disease to be treated by replacement—thyroxine—was isolated by Kendall, and that war was well behind us before to-day's chairman, Dr. Harington, made a new landmark in this application of chemistry to biological problems by determining the structure of thyroxine and making it by synthesis. Many, of course, of these chemical achievements have helped to turn the page to further fascinating chapters of research in experimental physiology and biochemistry—as by providing clues, for example, to a new understanding of enzyme-coenzyme systems, on which depend essential component reactions of the life-process. Chemistry has also made a beginning in the production of artificial substances of relatively simple structure but with activity so nearly identical with those of complex hormones as to enable them to replace the latter effectively in therapeutics (cf. stilboestrol, hexoestrol, etc.). Perhaps we get the most impressive idea of the completeness and the rapidity of the change which has occurred in the therapeutic outlook in this direction by recalling that, when the first world war began, the nature of diseases such as rickets and pellagra, widely prevalent in large communities, was still completely mysterious—we did not even know that they were diseases of dietary, or indeed of any kind of deficiency—and that before the second world war broke out chemistry had achieved the artificial production of the missing dietary factors, or vitamins, needed for their complete prevention or treatment.

I must make only passing mention of another kind of specific treatment in which natural immunological methods were employed against diseases due to infections by bacteria. This also had its beginning before the nineteenth century ended. Though it has undergone extensive and practically important developments, which have in recent years tended more and more to the side of preventive treatment, I think it can be said that chemistry, whether physical or organic, has only begun as yet to unravel the fascinating tangle of its complexities. Researches such as those of Oswald Avery and his colleagues, of the late Karl Landsteiner, and of Linus Pauling give abundant assurance, however, of a rich harvest for chemistry from further cultivation of this field.

A New Quest

I am going to ask your attention in rather greater detail to the remarkable and even exciting developments during recent years in the specific treatment of the causes of infection, the direct suppression of the infective agents, by administration of remedies which are artificial products of chemistry or in any case unnatural to the infected human or animal body—the method of which the pioneer, the first and most determined advocate, and the inspiring genius was Paul Ehrlich. Pharmacology at the beginning of the century dealt almost entirely with the effects of drugs on the symptoms. There were a few exceptions—mercury, used since the fifteenth century for a specific treatment of syphilis; cinchona (quinine) and ipecacuanha (emetine), used since the seventeenth century for the specific treatment of malaria and amoebic dysentery respectively. Ehrlich determined to lead a new quest for remedies, and particularly artificial ones, which dealt with the causes of infections, and he called it "chemotherapy." His conception of the process, as Ehrlich's ideas were apt to be, was picturesque and diagrammatic: he was going to find substances with a maximal affinity for what he pictured as "chemoreceptors" of the infecting parasite and a minimal one for those of the tissue cells of the patient.

It was natural to direct the search first to the discovery of remedies for protozoal infections, since the evidence appeared to show that the body did not protect itself against these by an effective reaction of immunity. There seemed, for example, to be no adequate production of antibodies against the protozoal parasites responsible for malaria. Ehrlich, who with his cousin Carl Weigert had been a chief agent in the introduction of the use of the synthetic dyestuffs into medical histology, had actually tried an experimental therapy of malaria with methylene blue as early as 1891, basing the attempt on its specific affinity for the malarial parasites as visible in a stained film of blood, and on his knowledge, from other researches, of its relatively low toxicity. This attempt, not wholly successful, led no further, probably because of the limitation then of experiments on malaria to the naturally infected human subject. Only later, after Ehrlich's death, with the use by others of the malaria-like organisms which infect birds, did progress ultimately begin in the chemotherapy of the malarial fevers of man.

The effective beginning of modern chemotherapy was made with diseases due to trypanosomes, infection with which Mesnil and Nicolle had shown to be transmissible in endless series in rats or mice. Ehrlich seized the opportunity offered, and, following with Shiga the line of his established interest in the dyestuffs, found the benzidine dyestuff trypan-red as the first effective cure for such an infection in mice. Trypan-red is now only of historical interest, but it provided the starting-point, not only for all modern chemotherapy, but for the particular line of advance that led to "germanin" ("suramin"), the most effective, on the whole, of remedies for trypanosomiasis yet discovered.

Since this new and effective beginning nearly forty-five years ago chemotherapy has of course extended widely and occupies a position of outstanding and still rapidly increasing importance in the treatment of infections. We have not time for more than a glance at a few of the other lines of research in this field which have led to important practical success. The discovery by Thomas and Breinl, in Liverpool, of the activity of the organic derivative of arsenic, atoxyl, on experimental trypanosomiasis in small

animals, gave Ehrlich and his co-workers a new starting-point for researches on the chemotherapy not only of diseases due to trypanosomes but of others, and even more generally important ones, due to spirochaetes. The culmination of this line of advance was in "salvarsan" (arsphenamine) as a remedy for syphilis, relapsing fever, and other spirochaetal infections, with, more recently, the use of the arsenoxide from which Ehrlich and Bertheim had actually made salvarsan by reduction, but which Ehrlich had put aside as too toxic, apparently from lack of a sufficiently systematic trial of suitable methods for its administration.

We have seen that Ehrlich's first abortive attempt at a better chemotherapy for malaria was made with methylene blue, which proved to be no satisfactory competitor with quinine, which, since the introduction of cinchona from South America to Europe in the seventeenth century, had been used empirically for the specific treatment of malarial fevers long before their nature was known. Apart from this very important application, quinine had of course been used in relatively trivial dosage for the routine and domestic treatment of a large range of febrile conditions on which it had no specific action. It was very fortunate that some years before the recent war, clues furnished originally by consideration of the structures of quinine and methylene blue had led research workers for German industry to the discovery, by experiments on malaria-like infections of birds, of one substance, "atebrin" (mepacrine), which was at least as effective against malaria as quinine, and that an intelligent anticipation of what might be coming had led to the manufacture in England and in the U.S.A. of sufficient quantities of mepacrine to meet the need before Japan had seized the cinchona plantations on which the world depended for quinine. Then followed a vigorous and organized campaign of co-operative research in Britain and the U.S.A. Chemists in a large number of academic, official, and industrial laboratories produced substances for trial on different types of malaria-like infections in birds, and eventually, in a few favourable cases, on malaria in man. The evidence yet available seems to give the first claim to a relatively simple substance named "paludrine" (Curd, Davey, and Rose), with a chlorphenyl group attached to a diguanidine nucleus, for superior activity in both prophylaxis and treatment of malaria over any remedy hitherto available, together with a remarkable freedom, in dosage effective for such purposes, from any toxic effects. And if such a result could be achieved in a few years under pressure of wartime necessity there seems no reason to assume that something even better may not be within reach of further effort. The chemical research leading to paludrine has given what may be a very important clue in the strong suggestion it affords of an association of antimalarial activity with groupings susceptible of tautomeric changes.

The Sulphonamides

Those must suffice as examples of the success of chemistry in producing such specific remedies for infections with protozoa and spirochaetes, though there are several others which could be cited if time allowed. For many years, by contrast, synthetic chemistry had a conspicuous lack of success in discovering analogous artificial remedies for the bacterial infections more familiar to ordinary experience in temperate climates—pneumonia, septicaemias, and the rest. There appeared, indeed, to be plenty of excuse for the long-prevalent outlook which had almost accepted the view that the methods of chemotherapy were inapplicable to bacterial infections and that the specific treatment of these must be left to immunological agents. Then in 1935 there was a sudden and dramatic change in the situation. Domagk's "prontosil," and the sulphanilamide found by Trefouel, Bovet, and Nitti to be its effective moiety, were soon established by clinical trials in this country, in the U.S.A., and then in all the world to be highly effective against streptococcal infections in particular, and for the first time conditions like streptococcal septicaemia following childbirth came under effective treatment. Then came the first preparation by Ewins and Phillips of the first derivative of sulphanilamide—sulphapyridine—with a sufficient enhancement of activity to make it effective against pneumonia (pneumococcus) and cerebrospinal fever (meningococcus), as discovered by Whitby. A series of others followed in rapid succession: some, such as sulphathiazole and sulphadiazine, with a generally higher effectiveness and lower toxicity; others, like sulphaguanidine and sulphasuxidine, owing their special use to the restriction of their actions largely to the bowel and its lining membrane, having particular effectiveness in the treatment of bacillary dysentery; yet others suitable only for local application to infected wounds. In their different ways and various applications it is not too much to say that, with the production of this series of sulphanilamide and its derivatives coming just when it did, chemistry, working in alliance with experimental medicine, had changed the whole aspect of the treatment of wounds and diseases of campaign, in the war which was to follow within a few years of the primary discovery. And we have only to look back to the available methods of dealing with the serious bacterial infections before 1935 to recognize the revolutionary change which chemistry, in its applications to chemotherapy, has also produced in the prospect of sufferers from these bacterial infections under the normal conditions of peace.

The discovery of substances with such a potent remedial action against infections by bacteria, which can so readily be maintained in culture on artificial media, provided new possibilities also for investigating the fundamental nature of the chemotherapeutic process. It soon became clear that the action of sulphanilamide and its derivatives, even in concentrations much greater than could ever be produced in the body fluids of the patient, was not to kill the bacteria but simply to suspend their multiplication, the curative effect in the living body being therefore not due to a direct killing of the infecting organisms but to a restrictive action on their power of growth and invasion, sufficient to tilt the balance in favour of the natural defences of the body. Chemistry has further provided at least a first hint of the nature of this bacteriostatic action. From bacteria susceptible to the action of sulphanilamide a substance could be extracted which, if present in sufficient concentration in the culture medium, neutralized the bacteriostatic action; and this was identified by Woods as *p*-aminobenzoic acid.

It seems likely, then, that sulphanilamide and its derivatives can somehow preoccupy the position, in relation to some enzyme system concerned with growth and multiplication of the organisms, that *p*-aminobenzoic acid would normally fill, and can thereby suspend the growth process. This can be only a part of the story, since other quite effective bacteriostatic agents, not distantly related in general molecular configuration to sulphanilamide, are unaffected in activity by the presence of *p*-aminobenzoic acid. Nevertheless, I think we can conclude that observations like those of Woods are opening the way to an interpretation of the action of the substances, and eventually of a much wider range of chemotherapeutic actions, in terms of chemically rational conceptions instead of in those hitherto current, which, in some cases at least, have been little more than impressive or picturesque labels for the unknown. There is a fascinating field here still inviting patient exploration,

and I venture to hope that we—medical biologists and chemists alike—shall be able to resist the temptation to simplify the problem unduly and to accept too easily as a solution a correspondence which may be no more than an indication, though a most valuable one, of the nature of *one* of the factors involved in a much more complex mode of action. Meanwhile any hint is of value which will give chemistry a rational clue to follow in this quest.

Penicillin

Hard on the heels of the revolution in the chemotherapy of the bacterial infections came that due to the renewed investigation by Florey, Chain, and their co-workers on penicillin, the existence of which had been made clear by Fleming's observations ten years earlier, and which had then dropped almost out of memory after a tentative chemical investigation by Raistrick had revealed its acidic nature and solubilities, but had suggested a baffling instability under conventional procedures for its separation. The story of how such difficulties were overcome, of the extraordinary potency and harmlessness of penicillin revealed by freeing it from undesirable concomitants, of large-scale manufacture rushed ahead to meet war's needs, the constitution of the now several penicillins determined by a great co-operative effort of British and American chemists and even confirmed in one case by an artificial synthesis (De Vigneaud)—all this is one of the almost romantic scientific achievements of chemistry, working in close alliance with medical biology, attained under the stimulus of the needs of armies in the recent war. And the magnitude of the opportunity now open to chemistry in this new field of antibiotics can as yet be no more than a matter of hopeful speculation.

Symptomatic Treatment

In the time at my disposal, even one aspect of the rapidly expanding service of chemistry to scientific therapeutics which I have chosen for special mention can only be presented thus in selective sketches with but little detail and with no attempt to make the presentation inclusive. There is only time left to me, before I conclude my lecture, to make it clear that, while I have specially dealt with the elimination of the causes of disease as a relatively novel aim and achievement of therapeutics, made brilliantly selective by an alliance of growing intimacy with chemistry, I am by no means depreciating the importance of the alleviation of symptoms. In this direction, also, chemistry has been furnishing a wealth, even in some directions an embarrassing excess, of alternatives—competitive ranges of hypnotics, analgesics, local anaesthetics, diuretics, laxatives, and so forth. And if anybody should doubt the real value, on balance, of the service which chemistry, with intelligent medical use of its gifts, has thus rendered to the ease and the safety of afflicted humanity let him go, for an impression of contrast, to any friend who has had the experience of anaesthesia for operation two or three decades ago and again in recent years. Nor, I think, can it be doubted that in this field of symptomatic treatment again a strengthening collaboration is enabling both chemistry and pharmacology to replace a shallow empiricism by an ever stronger foundation of scientific understanding. If I may be allowed to mention two examples, which have caught my special interest as having some relation to physiological studies of my own, we have recently seen the emergence of a series of synthetic pharmacological antagonists to histamine for the treatment of asthma and other allergic manifestations, and, even more recently, the use of D.F.P. (di-isopropyl-fluorophosphonate), a potent and permanent antagonist of cholinesterase, to relieve the dangerous post-operative paresis of the intestines.

ANOMALOUS MANIFESTATIONS OF MALNUTRITION IN JAPANESE PRISON CAMPS

BY

R. G. S. WHITFIELD, M.R.C.S., L.R.C.P.

Late Surgeon Lieutenant-Commander, R.N.V.R.

In a leading article in the *British Medical Journal* of June 22, 1946 (p. 958), the following passage appeared: "But in the Tropics and in war-stricken European countries field workers have demonstrated repeatedly that the clinical picture shown by malnourished or starved populations may often differ widely from textbook descriptions. As Stannus has pointed out, unknown or ill-defined deficiency diseases probably far outnumber those whose characteristics are already plainly established." Nearly four years in eight Japanese prison camps convinced me of the truth of these remarks, and three clinical conditions are described as illustrations.

Diet

Dietetically the period falls into two divisions:

1. *White Rice Period (January to October, 1942).*—Rice (polished), about 10 oz. (280 g.) daily; wheat flour (white), about 8 oz. (230 g.) daily; sugar, about 1 oz. (28 g.) daily; taro root and sweet potatoes, 4 oz. (115 g.) sometimes; vegetable soups of spinach, turnip tops, chrysanthemum leaves, onions, cabbage, about 8 oz. (uncooked); vegetable oil, about 1 oz. daily for frying; meat, fish, whale, approximately 3 oz. (85 g.) three times weekly until June, then diminishing. The daily diet is summarized approximately in Table I. There were almost certainly deficiencies

TABLE I

	Calories	Protein (g.)	Fat (g.)	Vit. A (I.U.)	Vit. C (mg.)	Thiamine (I.U.)	Nicotinic Acid (I.U.)	Riboflavine (I.U.)
Normal requirements	3,000–4,000	100	100	5,000	75	2,000	23,000	1,600
Probable minimum requirements	2,000	30–40	20–30	2,000	15	900	10,000	1,000
1942 diet ..	1,800	40–45	30	3,400	35	500	250	700

in pantothenic acid and pyridoxine (vitamin B_6), and possibly in biotin, vitamin E, and folic acid.

2. *Barley and Bean Period (November, 1942, to August, 1945).*—Whole-grain barley and millet were substituted in the rough proportion of three parts barley, one part millet, and one part polished rice. Meat—usually rancid pork—2 oz. (57 g.) monthly; fish, 4 oz. (115 g.) monthly; seaweed, 40 g. daily. Other foods according to season were the usual Western vegetables, plus daikon (a sort of giant radish-turnip), daikon tops, soya-bean paste and curd, sweet potatoes and tops, taro roots, egg-plant, pea-pods, bracken stalks in brine, dried octopus, snakes, wasp grubs, and the pupae of silkworms ("1 pupa = 2 hen's eggs"—any Japanese). Soya beans were issued fairly regularly and were our most valuable food. Deprivation always produced an increase of sickness. The calorie value varied from about 3,000 (1943) to 1,500 (1944). Thefts of food by the Japanese and the prisoners, and the unbelievable trading in food that went on, made it impossible to know how much was being eaten; and because of the intermittent and, in many cases, constant diarrhoea, together with the unexplained nocturnal diuresis, we could not estimate what was being absorbed. The unreliability of Japanese vitamin B injections (prepared from yeast or rice

polishings—the thiamine content was stated by only one manufacturer), too, made it impossible to decide what therapy was being given.

The "Painful Feet" or Gopalan Syndrome

(Hong Kong and Shinagawa, Tokyo, 1942–3)

On the white-rice diet the expected loss of weight, accompanied by weakness, bradycardia, hypotension, and constant "black-outs" on change of posture, soon became universal, and pellagrous dermatitis was not uncommon. After about five months men began to report with painful feet. I met many P.O.W. and Japanese doctors, but none had seen such cases before. The existence of a new syndrome, however, cannot be denied. It occurred in the Philippines, Malaya, Hong Kong, and Japan, and has been described by Stannus (in 1936), Jackson (1946), Page (1946), and others, and elucidated as a deficiency of pantothenic acid by Gopalan (1946). It appears probable that at least some of the cases reported by Ekbom and by Purdon Martin (1946) and described under the name of "jittery legs" in an annotation in the *B.M.J.* (1946) were early cases of pantothenic acid deficiency; for in England a non-bread-eater who disliked liver, kidneys, mushrooms, and peas might well be on the threshold of such a deficiency. It may therefore be worth while to describe the syndrome again.

A feeling of tiredness in the feet develops in a week or so to a vague discomfort mainly at night time. In about a month three symptoms appear: (1) a deep ache starting from the ball of the foot and spreading to the toes and instep, which is described as "like a toothache"; (2) a superficial burning sensation starting in the sole of the foot, quickly reaching the toes, and gradually involving the whole foot; (3) "pins-and-needles"—difficult for the patient to locate in the foot, and varying from "funny-bone" sensation to electric shocks. Occasionally an early case would get relief from heat, but developed cases unanimously sought cold. The pain was worse at night, and most men slept with their feet outside the blankets either because they could not bear the weight of them or, more commonly, because they craved the cold, despite indoor temperatures of 12° F. (−11° C.). The third symptom soon progressed to excruciating bouts of shooting pains up and down the feet and calves. The syndrome took about four months to develop fully.

I cannot exaggerate the sufferings of these men. By December, 1942, out of a total of 300 prisoners there were over 40 cases, and these were driven almost out of their minds. Two very dour tough Scotsmen used to spend every night sitting with their legs in a tub of water in which lumps of ice were floating, their bodies swathed in blankets and coats; and every evening some pain-wracked skeletons would beg for morphine to give them enough rest to carry on for a few nights. Unable to get any treatment for them except 0.5 mg. of vitamin B a week, I sent some twenty patients to a Japanese military hospital, where they were given lumbar punctures by medical students and received beatings on the feet. Several lost their toes through gangrene, and two had leg amputations. One committed suicide, and seven died from neglect.

Physical Signs

Soon after the onset a sharply delimited hyperhidrosis of the affected parts appeared, and the intense hyperaesthesia of the feet was gradually replaced by an ascending skin analgesia with complete insensitivity to pin-prick and cotton-wool, often to above the knee. First the ankle-jerks and then the knee-jerks, after some increase, slowly diminished, but complete absence was rare and occurred only after a year or so. Advanced cases showed loss of passive movement sensation, and the finger–nose and toe–knee tests became mildly inaccurate. These neurological findings, also recorded by Jackson and Page, contradict those of Gopalan, who specifically differentiates this syndrome as showing brisk knee-jerks, with no loss of sensation or of muscle power and no wasting or foot-drop. It is my opinion that these signs were produced by a concurrent deficiency, perhaps of thiamine, causing a peripheral neuritis (Gopalan's cases were on parboiled rice, which ensured an adequate thiamine intake), and do not in any way invalidate his description. With Gopalan's negative findings I am in entire agreement: there was no muscle-wasting or loss of power (apart from general emaciation), no foot-drop, no Rombergism, no ataxic gait (except that caused by the pain of putting the foot to the ground), no tenderness of the calf muscles, no spasticity, and no loss of superficial reflexes.

Page mentions that definite circulatory impairment was present. This was a late finding, which I feel should be attributed to the prolonged inactivity due to pain, the universal freezing therapy, and the generally impaired circulatory state rather than be considered as an organic part of the syndrome. And Graves (1946) said of the Singapore cases: "I submit that the later signs [in Page's cases] were dependent upon climatic conditions. Our chronic cases continued in the same state for many weeks or months, perhaps developing other of the deficiency syndromes such as retrobulbar neuritis or a spastic paraplegia, but never cyanosis of the limbs, gangrene, etc."

During the second half of 1943 most cases in Shinagawa camp started to improve slowly, both because of the quantities of stolen food brought into the camp and because soya beans and barley have the high pantothenic acid content of 18 and 20 μg. per gramme respectively. Also "refection" may have been occurring.

Associated Ariboflavinosis.—As with Gopalan, nearly every case showed or had shown an eczematous dermatitis of the scrotum, a painful tongue, angular stomatitis, and, less commonly, cheilosis in the form of dry crusting and fissuring of the vermilion of the lips (angular blepharitis was rare). Photophobia of bright sunlight with lacrimation and a feeling of grit in the eye, and conjunctival injection, were common every summer. Seborrhoeic dermatitis of the alae nasi, eyelids, and ears was not seen, nor was there any loss or greying of the hair.

Associated Oedema.—A common but not invariable association was oedema of the ankles or face, or both, without ascites or pleural effusion. One interesting case was that of a most reliable uncomplaining man who was suffering from severe painful feet. Overnight he developed considerable oedema of the feet and ankles and the pain left him entirely. His was a unique case, and I can suggest no explanation. This oedema was generally considered, despite a very small salt intake, to be due to hypoproteinaemia, and was contrasted with the oedema of wet beriberi, which, supposedly caused by lowered tone of the arterial walls and increased tension in the capillaries, is associated with warm extremities, flushed colour, and a feeling of firmness to the fingers (Bicknell and Prescott, 1946). But often cases would respond to injections of Japanese vitamin B coupled with oral yeast, while extra protein in the shape of meat, fish, or a Red Cross parcel did not seem to help. I never felt capable of differentiating between the oedema of beriberi and that of hypoproteinaemia (if there are two kinds), and it is interesting to note that Keys *et al.* (1946), investigating a group of thirty-four men on a "famine" diet with an average of 49 g. of protein, found that, although oedema appeared in all of them, the decline in the plasma protein concentration

averaged only 0.73 g. per 100 ml. (normal 7–8%; believed critical level for oedema 5%). They believe that famine oedema is not due simply to hypoproteinaemia or to renal or cardiac failure but probably to an abnormality of the capillary wall. Meanwhile Selby and Golberg (1946) have reported successful treatment with folic acid (which was probably deficient in our diet).

Many men developed loss of vision with a retrobulbar neuritis. It is noteworthy that the thirty worst cardiac cases (Table II) did not show very pronounced visual

TABLE II.—*Details of the Worst 30 Cardiac Cases, Mitsoshima Camp*

Diarrhoea		30
Peacetime alcohol consumption	T.T.	6
	Moderate	18
	Heavy	6
Average weight loss since capture		32 lb. (14·5 kg.)
Precordial pain	Yes	22
	No	8
Audible murmurs		3
Pulmonary second sound increased		10
Pistol-shot murmurs over femoral artery		0
Ectopic beats	Yes	15
	No	15
Pulse rate (recumbent)	40–50	1
	50–60	8
	60–70	6
	70–100	8
	100–120	3
	120–140	3
	140–150	1
Oedema on admission (i.e., ambulatory)	None	10
	Face and feet	18
	Feet only	1
	Face only	1
Average number of weeks since cutting	Toe-nails	14
	Finger-nails	10
Pain on pressing calves	0	7
	+	11
	+ +	9
	+ + +	3
	+ + + +	0
Analgesia of legs to pin-prick	Stocking type	18
	Patchy	11
	Nil	1
Knee-jerks	Increased	6
	Normal	9
	Diminished	12
	Nil	3
Ankle-jerks	Normal	11
	Diminished	14
	Nil	5
Visual acuity	6/5	2
	6/6	9
	6/18	11
	6/24	2
	6/36	5
	6/60	1
	Worse than 6/60	0

deterioration, and none of the worse cases of visual loss were included among them. The causative factor was plainly not identical with those producing the Gopalan syndrome, oedema, pellagra, or beriberi.

A Cardiac Epidemic

(Mitsoshima; Winter, 1944)

In June, 1944, Mitsoshima camp was emptied and refilled with 100 British direct from the infamous Thailand Railway (all were emaciated and most had malaria) and 100 Americans from a copper mine near Tokyo in moderate condition. The Japanese immediately cut the food, increased the work, and embarked on a campaign of systematic brutality. The health of the camp deteriorated rapidly. By September weakness, especially of the legs, was general, oedema was common, and complaints of painful feet were starting. Of 213 men, 60 were suffering from evident malnutrition by the beginning of October, 74 by November, 90 by December, and 142 by the beginning of January. In December a survey of the entire camp was made (Table III).

From Dec. 20 to 30, 1944, with an astonishing unanimity of timing, 30 cases of severe cardiac involvement reported —21 British and 9 American. Following two sudden deaths we were allowed to send over 60 men to hospital. Certain features are worthy of comment.

TABLE III.—*General Survey of Mitsoshima Camp at end of December, 1944*

No. of men in the camp		213
Failure of vision (81 cases)		
Mild (up to 6/18)	Without other signs of malnutrition	9
	With " " "	26
Severe (up to 6/60)	Without " " "	3
	With " " "	37
Very severe (letters visible only a foot or so distant; all with other signs of malnutrition)		6
Oro-genital syndrome (12 cases)	Dermatitis of scrotum only	7
	Sore tongue only	5
Painful feet (124 cases)	Moderate	104
	Severe	20
	Very severe	0
Some anaesthesia to pin-prick		74
Oedema		77
Diminution of leg reflexes		50
Complaining of shortness of breath		74

1. All the cardiac cases except one appeared in the space of ten days, despite the better physical condition of the Americans.

2. The paucity of physical signs made it difficult to assess the clinical condition. Pain in the feet was in no case as severe as in the 1941–2 period, and the oro-genital syndrome was much rarer. No textbook case of beriberi was seen, but a peripheral neuritis developed similar to that at Shinagawa, except that the skin anaesthesia was markedly patchier and less "stocking" in type, and tenderness of the calves was fairly common. There was no obvious correlation between severity of the neuritis and the cardiac condition. We tried to assess the cardiac condition by means of an exercise-tolerance test of twelve full knee-bends—where it seemed safe. Surprisingly, all the men did well at it, and the pulse rate was nearly always back to normal after two minutes, even though many were too weak in their thigh muscles to manage the full number. As there was no infallible herald of approaching cardiac crisis the prognosis of each case had to be modified frequently. To give or withhold our limited American thiamine was a heart-breaking decision, made on clinical intuition rather than on physical signs.

3. The symptoms were unvaried: sudden weakness of the legs, causing the astonished patient to sit; generalized exhaustion; a consciousness of palpitation and often irregular beats; breathlessness on exertion; and nocturnal attacks of palpitation which woke up the patient sometimes with pain and always with intense anxiety and dyspnoea, partially relieved by sitting up, as in cardiac asthma.

4. All except one case showed delay in nail growth (not found in Shinagawa). Hair growth was affected in only one man who had very severe neuritic signs, and his beard grew at one-third the normal rate. One common finding was the loss of hair on friction areas on the legs. This seems to contradict the findings of Castellani, quoted by Sutton and Sutton, of hypertrichosis of malnutrition affecting especially the legs of boys and girls and returning to normal on adequate diet. Two cases had perforating trophic ulcers of their toes, unknown to themselves.

The treatment of all cases was the same: 12 American "multivite" tablets by mouth a day, each containing 1 mg. of thiamine. Intravenous vitamin B was reserved for emergencies and those with severe diarrhoea. All cases received these until apparently out of danger, and many took 300 to 400 tablets. Yet the response was disappointingly slow, even allowing for poor absorption. Two deaths occurred on Dec. 27 with the usual signs of right-sided failure. American thiamine, 50 mg., was given intravenously, venesection was performed, and digitalization was attempted. On March 17 the Japanese forced a group of light-duty cardiac cases out to work. At lunch-time they were exhausted, and we were allowed to put them in hospital. At tea-time one of them, who had been resting uncomplainingly, died in three minutes. Six days later another died of general weakness, with low-grade bronchopneumonia. One more death occurred in July—that of a man doing normal work, with no symptoms other than a chronic oedema. He returned to camp one mid-morning with dyspnoea. Intravenous thiamine was started, but he died three hours later, his apex beat having moved 1½ in. (3.8 cm.) outward in that time.

The thiamine content of the diet at this period was around 1.5 mg. daily and the calorie intake about 2,000. According to Cowgill's formula the daily requirement would be only just over 0.5 mg. But against this must be balanced the low protein and the low or absent fat intake, the poor absorption due to diarrhoea, the very hard work, and the fact that many workers consider his formula an underestimate.

Was thiamine deficiency responsible for these cases? The experiments of Williams *et al.* (1940, 1942, 1943) on women volunteers in controlled thiamine deficiency are strikingly parallel. These women lost weight, were fatigued and giddy, and had faint heart sounds and lowered blood pressures, with tachycardia and sinus arrhythmia on exertion. Their calves were tender and the squatting test was impaired. But two findings which these authors emphasized were absent. The first was anorexia. In their cases this started after thirty days, developed into nausea and epigastric distress with occasional vomiting in fifty days, and by seventy days there was constant nausea. At Mitsoshima vomiting was seen only in acute food-poisoning, while hunger was so constant that scavenging of the kitchen refuse was a grave problem. Epigastric distress did not occur. His second finding was mental changes suggestive of neurasthenia, the subjects becoming depressed, quarrelsome, and fearful. They lost interest in reading, were confused in thought, and lacked manual dexterity. All these symptoms, except perhaps a slight impairment of memory, were conspicuously absent in Mitsoshima. One cardiac case developed thickness and slowness of speech and mental retardation, but recovered slowly on treatment. These cases, then, can hardly have been pure thiamine deficiencies. Clinically they resembled cardiac beriberi, except that they responded poorly to vitamin B and had none of the typical nervous lesions. (Anorexia and memory defects are quite common but not invariable in beriberi.)

A Visitation of "Fits"

(Mitsoshima; Spring, 1945)

Epileptiform seizures affected four men in the course of six weeks. Three were pyknic in build, powerfully muscled, and well covered with fat. The fourth, mentioned before as having delay in beard growth and marked neuritis, was tall and extremely emaciated. In common they all had insatiable appetites, the thin one being a thief and garbage scavenger. Table IV summarizes the physical condition of these men.

TABLE IV.—*Epileptic Cases*

No.	Nationality	Build	Vision L.	Vision R.	Oedema	Knee- and Ankle-jerks	Anaesthesia	Other Evidence of Malnutrition
1	American	Thin	6/18	6/18	Nil	Nil	Marked; patchy up to knee	A severe cardiac case, in bed for weeks
2	"	Fat	6/36	6/24	Face, slight	Normal	Nil	Quite fit
3	"	"	6/18	6/24	Nil	V. slight diminution	Slight, patchy, of feet	Complained of great tiredness
4	British	"	6/18	6/9	Face and ankles, slight	Normal	Nil	Scrotal dermatitis

Case 1.—On April 17, 1945, while the patient was lying down after a copious vomit, tonic convulsions started without warning. He was deeply cyanosed, with trismus; the back was arched in opisthotonos and the pulse was almost impalpable and about 40. The pupils were widely dilated and equal, and the hands were in tetanic spasm. He voided urine but not faeces, and did not bite his tongue. The plantar response was normal. The tonic stage lasted so long that death seemed inevitable, but it was succeeded by a short clonic phase which lapsed into profound slumber with hissing respiration suggestive of "air hunger." He could not be roused. The urine was strongly acid to litmus, but when tested with some Japanese reagent was negative for sugar. As the nature of this reagent remained a mystery the presence of ketone bodies in the urine must remain open to question. There was no history of epilepsy for the preceding three years. The enormous black liquid vomit turned out to be an infusion made from sarsaparilla gathered outside the camp, but as there was no rubber tubing it was not possible to wash out the stomach. It seemed unlike a Stokes-Adams attack and the pulse rate started rising slowly. There was no history of malaria or nephritis, and the urine contained no albumin. Then a powerful smell of acetone was drawn to my attention (I am anosmic), and it seemed that we had a case of ketosis, perhaps due to starvation. Glucose, calcium, and dried plasma were given intravenously. Three hours later another and equally severe attack occurred and morphine was given. Six hours later there was a third attack, and his condition seemed hopeless. However, after twelve hours' sleep he awoke and seemed none the worse, except for feeling shaky.

Cases 2, 3, and 4.—Within six weeks the three fat men were affected with exactly similar attacks, all occurring while at rest or asleep. One had seven fits in twenty-four hours. Treatment was unchanged except for some sterile bicarbonate solution which we had made meanwhile. All recovered quickly once they emerged from their coma-like slumber, and felt fit for work again in forty-eight hours. There was no residual mental impairment. Only Case 2 had a recurrence—about three weeks after his initial attack.

Contrary to our expectations the heat of the summer failed to produce any more cases, and the little "epidemic" passed off as mysteriously as it had appeared. Why were only four out of 213 men affected in the period of six weeks? They had all received multivite tablets and seemed in no way different from the rest of the camp. Chick *et al.* (1938) produced epileptiform fits in pigs and rats by depriving them of pyridoxine (vitamin B_6), but it is difficult to see why these four men alone should suffer such a deficiency. It seems most likely that they were caused by a sudden ketosis with the formation of aceto-acetic acid. This could not have been exogenous, as there was no fat in the diet; but, in starvation, as the liver glycogen is depleted fat is converted in the liver to ketone bodies, which may be formed faster than the tissues can utilize them. There seem to be two objections to this: first, that except for the one thin man the patients were by no means starving; secondly, it is difficult to conceive of ketone bodies appearing too rapidly in the blood for premonitory symptoms to be felt as in diabetes. All four men started their attacks by copious vomit, so that perhaps fundal pressure on the heart produced vagal stimulation. But such a trigger mechanism could hardly have played any part in the successive seizures, as the distension had been relieved. The possibility that lack of vitamin B complex reduces sugar tolerance in diabetes may be relevant, although Wade (1947) has failed to confirm this in the particular case of nicotinamide.

Summary

Three conditions arising from malnutrition are described which did not behave in the manner laid down in textbooks.

On a diet of polished white rice, pantothenic acid deficiency with an accompanying peripheral neuritis was the chief trouble.

On a barley and bean diet, cardiac beriberi occurred with some pantothenic acid deficiency and a slightly different neuritis.

At no time was a typical case of dry beriberi seen.

A series of four cases of epileptiform seizures of unknown causation is described.

The wise humility of such authorities on deficiency diseases as Stannus is supported by clinical observations.

I wish to thank Dr. Wrigley, of Messrs. Roche Products, for procuring a copy of Gopalan's article and sending it out to me in Greece; and Dr. A. A. Weinstein, of Atlanta, Ga., for refreshing my memory of details of the "fits" episode. The food figures are taken from the "Nutritive Values of Wartime Foods," No. 14 of the M.R.C. war memoranda, or from Bicknell and Prescott.

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TEMPORAL OR GIANT-CELL ARTERITIS

BY

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Since 1932 reports have been published from time to time describing what appears to be an unusual form of arterial inflammation. This condition seems to have a particular predilection for the superficial cranial arteries, and so frequently have the temporal arteries been involved that it has been known as "temporal arteritis." More recently Cooke *et al.* (1946), in a masterly review of the condition and its literature which includes a full description of seven of their own cases, suggest that the condition is probably less rare than the literature suggests—only forty cases had been described up to 1946—and that its effects are not confined to the cranial vessels but may be widespread throughout the body.

Their histopathological findings differed little from those of other writers, and they describe a subacute inflammatory process which, starting in the adventitia, subsequently spreads axially to the media, and is accompanied by areas of necrosis in the media and interna elastica of such a nature as to suggest an obliterative process in the vasa vasorum. They confirm the finding of giant cells, which give to the condition one of its names. The appearance of these follows necrosis, differing in this respect from tuberculosis, in which they precede necrosis. There is nothing to support a tuberculous hypothesis when considering aetiology.

My observations support the thesis, so ably presented by these workers, that the condition is by no means rare and that its recognition is difficult unless the possibility is borne in mind, but easy when once seen or the clinical picture appreciated. I believe that the diagnosis will be made with ever-increasing frequency and that neurologists particularly may find it useful in answering a number of baffling problems. For these reasons I feel that at the present time reports should be made of cases as they appear, even if only individual cases can be recorded.

Case I

In July, 1945, I was asked to see a man aged 65 who had shown an unexplained temperature for over a month. Two years previously he had suffered from intermittent claudication in the left leg. This had not been severe, and had been in abeyance for over a year. Apart from this the patient, who had been an Army instructor in physical training, presented an excellent medical record. About six weeks before I saw him he had begun to experience lassitude, depression, and widespread pains about his body. He had lost his appetite, and after ten days retired to bed. His condition deteriorated, and sweating at night became pronounced, while severe headache made its appearance. At this stage he asked his doctor to visit him. Physical examination was negative, but it was found that fever up to 101° F. (38.3° C.) was present. This condition continued, and headache became very severe, preventing sleep. The Widal reactions were investigated and were found to be negative.

When first seen on July 29 his appearance was striking. He appeared ill and looked older than his age. His face was expressionless and suggested profound dejection, which was confirmed in conversation. Physical examination was unproductive, but it was noted that there was no pulsation in the left dorsalis pedis artery and that the left temporal artery and both facial arteries were thrombosed. Furthermore, they were exceedingly tender to the touch, as was the right temporal artery though it was pulsating. There was, in addition, tenderness in the occipital region and the patient explained that his head had been so sore that it was sometimes impossible to lay it on the pillow. The only other findings were an absence of the abdominal reflexes and exaggerated deep reflexes. The plantar responses were flexor. Heart and lungs seemed normal and the blood pressure was 150/90. The fundi were within normal limits. A tentative diagnosis of periarteritis nodosa was suggested and he was admitted next day to hospital.

In hospital further investigations were carried out. A skiagram of the chest showed no abnormality in the heart or lungs. Electrocardiograms were normal. The urine showed a trace of albumin, a few red cells and epithelial casts, and was sterile. The blood count revealed 5,000,000 red cells, 80% haemoglobin, and 6,600 white cells, with a normal differential count apart from an eosinophilia of 7%. The blood sedimentation rate showed a fall of 40 mm. in the first hour when estimated by Wintrobe's method. The blood urea was 42 mg. per 100 ml.; the Wassermann reaction was negative. Agglutinations for enteric and *Br. abortus* were negative. The cerebrospinal fluid was normal, except that 5 cells per c.mm. were present; the Wassermann reaction and the gold-sol curve were negative. Blood culture was sterile.

An inch (2.5 cm.) of the anterior branch of the right temporal artery was removed under local analgesia, and the microscopical appearances here were consistent with a diagnosis of temporal arteritis. The operation produced a remarkable alleviation of headache in this part of the head. During his stay in hospital the fever persisted, but there was a gradual improvement in his general condition. Headache was reduced, sweating became less severe, appetite improved, and he became rather less depressed. His haemoglobin level fell to 63% and his sedimentation rate continued high. Apart from symptomatic treatment he was given nicotinamide by mouth. He was discharged home to bed, where his improvement was maintained.

He was readmitted to the surgical ward at the end of November with gangrene of a toe on the left foot. I did not see him then, but the fact that his sedimentation rate was still high, though falling, suggests that the condition was active. He was apyrexial. A left femoral periarterial sympathectomy was carried out in an attempt to save the toe, but it was not successful and amputation became necessary later. Though no sections were cut off the arteries at the site of the operation it seems likely that the gangrene was due to arteriosclerosis obliterans and not to giant-cell arteritis. It will be recalled that he had suffered from intermittent claudication two years previously and that there had been no tenderness of the dorsalis pedis artery.

By June, 1946, the patient seemed perfectly well, and his wife assured us that he had suffered no ill effects as a result of his long illness. Furthermore, his blood picture was normal and the sedimentation rate only 4 mm. During his convalescence from the operative treatment there had been a period of mental confusion lasting several days. We did not see him in this state, and it is difficult to be sure whether or not this was

related to the drugs he was receiving or to cerebral ischaemia. Mental symptoms have from time to time been recorded (Cooke *et al.*, 1946).

Case II

On June 27, 1946, a man aged 65 was led into my consulting-room at the hospital; at once something in his general appearance recalled the case which has just been described. He was expressionless, dejected, and ill-looking. He had been well until April, when symptoms of lassitude, failing strength and appetite, muscular pains, sweating at night, and especially severe and increasing pains in his head, had appeared. There had also been an unproductive cough and he had lost weight. He told us that his head had been so painful that it was often impossible to tolerate contact with the pillow, and, in his own words, "the veins" of his head had been very tender to the touch. Three days before the consultation he had lost the sight of his right eye and within a couple of hours the left eye had shared the same fate.

On examination both temporal and both facial arteries were thrombosed and very tender, and there was tenderness on palpation over the occipital region. His fundi showed bilateral thrombosis of branches of the central retinal arteries with fragmentation of the blood stream, well seen in other branches. His abdominal reflexes were absent, but no further physical signs were discovered. The blood pressure was within normal limits.

He was admitted to hospital at once for fuller investigation. He was found to be running a temperature up to 100° F. (37.8° C.). Blood examination showed 4,800,000 red cells; haemoglobin 84%; white cells 9,000, with a normal differential count; blood urea 35 mg. per 100 ml.; blood sedimentation rate 43 mm. in the first hour (Wintrobe); Wassermann reaction negative. The urine showed a trace of albumin, a few red cells, and an occasional hyaline cast. The cerebrospinal fluid revealed no abnormality, and the Wassermann reaction and gold-sol curve were negative. Blood culture was sterile and the usual agglutinations were negative. A skiagram of the chest and skull revealed no abnormality and the E.C.G. tracing was normal.

An inch (2.5 cm.) of the right temporal artery was removed under local analgesia—a portion was cultured but grew nothing—and the histological appearances of the sections made were quite characteristic of temporal arteritis.

While in hospital he developed an area of superficial inflammation of the scalp along the distribution of the left temporal artery. This area was tender and persisted for about three weeks. His right plantar response became extensor for about a week and there seemed to be an exaggeration of both knee-jerks. His general condition altered very little; he remained febrile, quiet, and uncomplaining except when questioned; it was, however, clear that head pain remained severe, though it had been relieved in the region of the biopsy. He was given 1,000,000 units of penicillin in a week, but so far as one could say this had no effect upon his condition. At the end of a month in the ward fever remained at about the same level, his haemoglobin had fallen to 58%, and his blood sedimentation rate remained high.

When last seen on Aug. 28 he was showing considerable improvement. His headache was much less severe, his appetite was returning, and he was more inclined to talk. There had been no return of vision, and his sedimentation rate had fallen a little, to 35 mm. I have not seen him again, but I understand that he has continued to improve in every way except that he remains blind.

Case III

In September, 1946, I was asked to see a woman of 73 who had been in hospital for three weeks with an unexplained fever. This had remained between 100° and 101° F. (37.8° and 38.3° C.), and in spite of a very thorough investigation was still unexplained. She had been hypertensive for a long time, and had complained of severe cephalalgia for some three months. There had also been pain on moving the jaw, general lassitude, depression, and anorexia. The only positive finding on her investigation was a very high sedimentation rate. On examination she had tender facial, temporal, and occipital arteries, though pulsation was present in all these vessels. No biopsy was possible, but I have little doubt as to the diagnosis, and her subsequent slow but steady progress towards recovery fits in well with the condition under discussion.

Case IV

A man aged 67 was first seen early in 1946 suffering from symptoms characteristic of gastric ulcer. He had had similar attacks in the past, and the present symptoms cleared up well on routine treatment. Some three months later he was seen again on account of severe headache, pain in the right shoulder, and general weakness. There had been no recurrence of his dyspepsia. Physical examination was negative, but there was tenderness in the occipital region and over the course of the temporal arteries, though pulsation seemed normal. Investigations were not possible, and a tentative diagnosis of temporal arteritis was suggested. His symptoms altered little during the next six weeks, but at the end of this time he developed a complete right twelfth cranial-nerve palsy.

Mr. McKeith could find little amiss in his throat, and skiagrams of the skull and neck were normal. Two weeks later, by which time his twelfth cranial-nerve palsy had recovered very considerably, he was seen by Mr. Pennybacker, who, quite independently suggested temporal arteritis as a possible diagnosis, but in view of a sedimentation rate only a little raised he did not feel able to be dogmatic. A month later the patient suffered an acute perforation of a gastric ulcer high up in the lesser curve. Before operation it was noticed that his left radial pulse was absent. He did not survive the operation, and at a post-mortem examination the left subclavian artery was found to be thrombosed. There had been no recurrence of gastric symptoms before the catastrophe. Unfortunately no histological examination of the thrombosed artery was undertaken, nor was the arterial supply of the stomach in the region of the perforation investigated. It seems possible that an ischaemic process here may have resulted in ulcer formation and perforation.

Discussion

In a period of little more than a year four cases have been seen in which a diagnosis of temporal or giant-cell arteritis has seemed justified. In two of these biopsy produced incontrovertible evidence, while the other two were clinically most suggestive.

I feel that the clinical picture is sufficiently characteristic to suggest the diagnosis. The patient is always in the latter part of life—no case under 55 has been reported. He may have been in good health prior to the gradual onset of a subacute illness in which fever, severe cephalalgia, anorexia, depression, and general toxaemia figure prominently, and arthralgia, myalgia, scattered lesions in the central nervous system, and interference with vision are often seen. Physical signs depend upon the situation of the disease, but tender thrombosing arteries about the skull are an almost constant finding. A low-grade secondary anaemia is common; a slight increase in white cells, sterile blood culture, normal blood urea, negative Wassermann reaction, but almost invariably raised blood sedimentation rate complete the picture. Cooke and his fellow workers (1946) do not stress the high sedimentation rate, but record that it was noted by Bowers (1940), Sprague and Mackenzie (1940), and Murphy (1942). In three of my cases the figures recorded are very high and did not return to normal until a considerable time after symptomatic cure.

In considering diagnosis, the age of the patient is against the possibility of periarteritis nodosa, in which condition younger individuals are attacked and in which the visceral vessels suffer severely. A high blood urea is almost constant and mortality is high. In temporal arteritis, though visceral vessels are by no means immune, they suffer less constantly, nitrogen retention is unusual, and mortality is relatively low. Buerger's disease, appearing again at an

earlier age, attacks particularly the arteries of the legs and frequently results in gangrene.

The disease often lasts up to a year; it seems to be self-limited, and is rarely fatal. No specific organism has been discovered to be causative, nor does drug allergy appear to play any part, as seems so probable in periarteritis. From experience in one case, penicillin appears to be without effect. Cook *et al.* (1946) used nicotinamide in their cases, but were not impressed with its effect. I have wondered whether the use of the anti-coagulants heparin or dicoumarol early in the disease might not reduce the risk of permanent damage, especially in the brain and retina.

ADDENDUM

Since writing this note I have had the opportunity of studying a number of papers by American writers (Gordon and Thurber, 1946; Dantes, 1946; Shannon and Solomon, 1945; Hoyt, Perera, and Kauvar, 1941; Chasnoff and Vorzimer, 1944; Post and Sanders, 1944), and it has been striking how closely the clinical and pathological findings have approximated to one another in all the descriptions, thus confirming my impression that the syndrome is sufficiently characteristic to suggest the diagnosis to physicians who are confronted with it. All the writers agree as to age incidence, a prolonged subacute phase with low fever, progressive secondary anaemia, mild leucocytosis, and high sedimentation rate, during which the main symptoms, already named, are prominent, followed by a protracted stage of slow recovery, with reduction of symptoms and improving blood picture. All agree that the sedimentation rate falls relatively slowly and may still be abnormal after the main symptoms have disappeared. All agree, too, that the tendency is towards spontaneous recovery, and that mortality is low. Most writers note that the disease appears more often in women.

Shannon and Solomon (1945) record a case with permanent bilateral loss of vision, as was present in my second case. Hoyt, Perera, and Kauvar (1941) note the symptom of pain on moving the jaw. This symptom appears not infrequently, and was prominent in my third case. Post and Sanders (1944) stress the expressionless facies, and refer to a Parkinsonian appearance. This was very striking in Cases I and II, above. Many writers have described reduction in pain after arterial biopsy, though Dantes (1946) noted but little improvement in his case. Relief following biopsy was unquestionable in the two of my cases in which this was carried out. All writers agree that the aetiology remains obscure, and no useful therapy apart from arterial resection has been suggested. I can find no reference to the attempted use of anticoagulants.

I wish to thank Drs. Proverbs, Carling, Bowers, and Barnett, who referred to me the four cases here described; also Drs. Wrigley, Gleave, and Edwards, who were responsible for the pathological investigations.

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The Council of the International Organization for Standardization held its first meeting in Zürich on June 17–20 under the presidency of Mr. Howard Coonley, of the U.S.A. The Council consists of representatives from the national standards bodies of Britain, Australia, Belgium, Brazil, China, France, India, Norway, Switzerland, the U.S.A., and the U.S.S.R. Mr. Coonley is president of the I.S.O., and the Council appointed M. Henri St. Leger general secretary. It was recommended that the International Electrotechnical Commission should affiliate with the I.S.O.

ANASTOMOTIC ULCER 12 MONTHS AFTER SOMERVELL OPERATION

BY

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The following case, in which an anastomotic ulcer occurred twelve months after a Somervell (1942) operation and gastro-enterostomy, may be of interest.

Case Report

A man aged 44 began to suffer from painful indigestion in 1942. In April, 1944, he was discharged from the Army with a diagnosis of duodenal ulcer and pyloric stenosis. I saw him in November, 1945, when a clinical diagnosis of duodenal ulcer and recurrent appendicitis was made. The barium meal showed a small ulcer deformity at the incisura angularis, and the pyloric canal was displaced to one side of the duodenal cap—consistent with an old duodenal ulcer. The fractional test meal showed that the highest total acid and free acid were 50 and 40 respectively (Fig. 1). Operation was advised because of the history

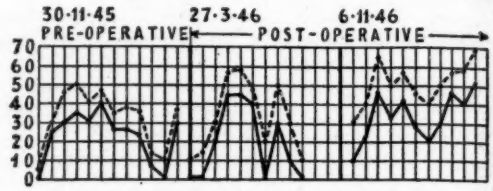

FIG. 1.—The pre- and post-operative acidity curves.

of having recently vomited food which he had taken the previous day, indicating impending stenosis.

First Operation.—On Jan. 1, 1946, the Somervell operation of ligature of all the gastric vessels and a posterior gastro-enterostomy was performed. The ligatures included the left coronary artery, the pyloric artery, and all the branches of the right and left gastro-epiploic arteries from the pylorus to the lower pole of the spleen (Fig. 2). He made a good recovery.

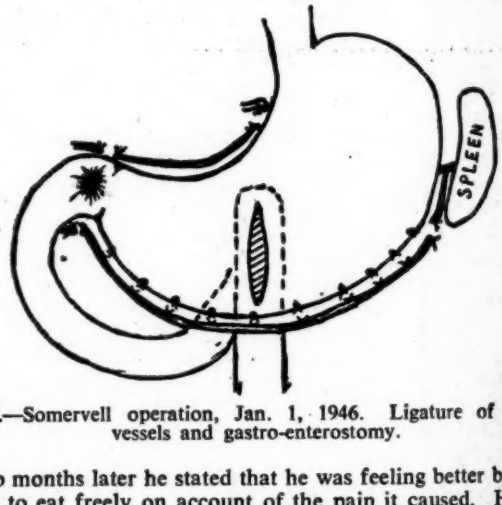

FIG. 2.—Somervell operation, Jan. 1, 1946. Ligature of gastric vessels and gastro-enterostomy.

Two months later he stated that he was feeling better but was afraid to eat freely on account of the pain it caused. He was putting on weight. A second fractional test meal showed that the highest total acid and free acid were 60 and 45 respectively, in contrast to the pre-operative figures of 50 and 40. In March he started work, his weight had increased by 2 lb. (0.97 kg.), and he was feeling well. When seen on Aug. 16, 1946, he complained of pain in the left iliac fossa, although it was not quite so severe as before operation. His abdomen felt sore. A barium meal showed a gastro-enterostomy deformity of the stomach, and the crater of a gastric ulcer just above the stoma. Operation was advised because of the pain from the increasing

acidity, and especially because, in my experience, if a patient has any sort of discomfort after a gastro-enterostomy he has almost certainly a stomal ulcer, and the sooner the anastomosis is undone the better. He declined this.

He returned in October, 1946, when he was "not feeling too good." He still had the pain, and his appetite was only fair. A third fractional test meal showed that the highest total acid and free acid were 70 and 52 respectively in contrast to the previous figures of 60 and 45 (see Fig. 1). Operation was again advised, and this time it was accepted.

Second Operation, November, 1946.—An enormous gastric ulcer was found, beginning on the stoma and passing widely up on to the lesser curvature, perforating into the pancreas as shown in Fig. 3, which is taken from the artist's painting of the

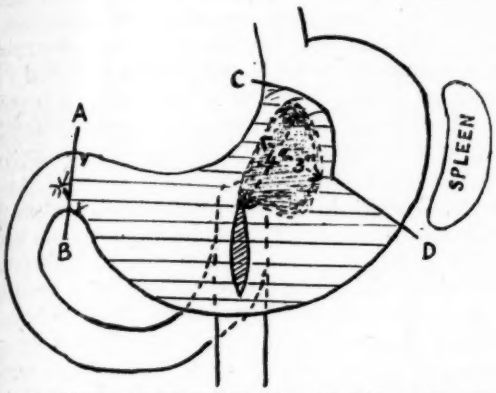

FIG. 3.—Findings at re-operation, Nov. 19, 1946. Lines A—B and C—D indicate area of stomach excised. The size of the ulcer is also shown.

specimen. It was approximately 3 by 3½ in. (7.6 by 8.9 cm.). A partial gastrectomy was performed (Fig. 4) and he made a good recovery.

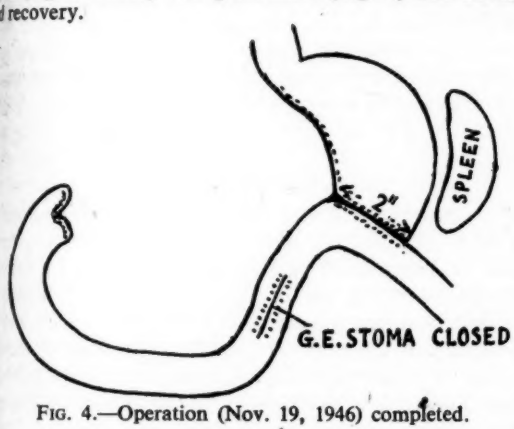

FIG. 4.—Operation (Nov. 19, 1946) completed.

Comment

The points I wish to present in reporting this case are: (1) This is the largest anastomotic ulcer I have seen in a personal series of 40 cases and certainly the quickest to develop after a gastro-enterostomy (twelve months). (2) The progressive increase in the acid content of the gastric juice is the opposite to that for which the operation is designed. (3) I have performed the Somervell operation for several patients with unimpressive results, and therefore offer the conclusion that, for London patients at any rate, the Somervell method offers no advantage. (4) Finally, in my experience, if a patient after a gastro-enterostomy is not completely comfortable, but needs to diet or to take powders, then the sooner the gastro-enterostomy is undone the better. A stomal ulcer is likely to be present, and in my patients it was seldom shown by the radiographs.

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THE COMBINED ACTION OF PHENOBARBITONE AND EPANUTIN

BY

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The two most important drugs in the modern treatment of epilepsy are phenobarbitone (5-phenyl-5-ethylbarbituric acid, "luminal," "gardenal") and "epanutin" (soluble phenytoin, sodium diphenylhydantoinate, "soluble dilantin"). It is only when the pharmacology, toxicity, etc., of these drugs are appreciated that they can be used with the maximum efficiency; I have dealt with this matter fully elsewhere (Blair, 1940). For the present it suffices to say that the chief disadvantage of the former is the drowsiness it may produce in adequate anticonvulsant doses, and of the latter the toxic effects (particularly those of a neurological, mental, or dermatological nature) when administered in doses of over three or four capsules (1½ gr.—0.1 g.—each) daily. A number of authors have tried these two drugs in combination in the hope that a synergistic action might occur.

The reports published to date (see Bibliography) have varied in their findings; some claim that in nearly all cases the use of epanutin and phenobarbitone together is more efficient than when these drugs are administered separately, but others find that in combination they are seldom better than when one or other is given alone. Moreover, little has been said regarding the frequency of toxic symptoms when they are combined, the optimum dosage in which they may be administered, etc.

In my experience there is a definite place in anticonvulsant therapy for the combined use of epanutin and phenobarbitone, and the present work was undertaken* to try to throw some light on the proportion of cases in which the combination of the drugs is more efficient than either administered separately (*a*) in controlling the number of fits and (*b*) in improving behaviour; the optimum dosage in which the two drugs may be combined; what toxic effects or other complications occur during their administration; and their pharmacological action.

Method and Results of Investigation

All patients concerned in this series were epileptic psychotics, mostly of long standing. For purposes of description the work may best be considered in three different categories: (1) the effect of adding epanutin in patients previously on phenobarbitone; (2) the effect of adding phenobarbitone in patients previously on epanutin; (3) a clinical trial of the two drugs combined in capsule form (referred to throughout this article as "E and P capsules").

Patients Previously on Phenobarbitone

In this group 30 chronic psychotics (whose ages ranged from 32 to 67 and averaged 42 years) had been on phenobarbitone for at least twelve months previously. Epanutin was added and the results observed. In a few cases previously on 3 or 4 gr. (0.2 or 0.26 g.) of phenobarbitone the dosage was reduced for control purposes to 2 gr. (0.13 g.) after epanutin had been combined with the former dose for several months.

* At Cane Hill Hospital in 1940–1 and not previously published owing to my absence on service in the R.A.M.C.

At first epanutin was added in a dosage of 1½ gr. (0.1 g.) twice a day. This produced no noticeable reduction in the number of fits. None of the patients showed any noteworthy change in behaviour or any digestive upset, but there was evidence of toxicity in one case which took the form of typical ataxia and confusion, and which cleared up as soon as epanutin was withdrawn. After three months on 1½ gr. of epanutin twice a day the dosage was increased to 1½ gr. three times a day, and this combination of drugs was continued for six consecutive months, at the end of which time epanutin was again gradually withdrawn. The results obtained were as follows. In five cases there was a definite decrease in the number of fits,* but in the rest the total number of fits remained, broadly speaking, unchanged. In eight cases an improvement in behaviour was noted (three in association with a diminution of fits and five with no change in their frequency). In each of these cases the diminished frequency of fits or improved behaviour ceased when the epanutin was withdrawn.

Five of the cases had toxic symptoms, but these were confined to the nervous system and took the following form: ataxia, 1 case; confusion, 1; ataxia and confusion together, 2; paraesthesia, 1. All cleared up on withholding the epanutin.

In one of the two control cases in which the phenobarbitone had been reduced from 3 to 2 gr. (0.2 to 0.13 g.), and in all three cases in which it was reduced from 4 to 2 gr. (0.26 to 0.13 g.) (all cases being on 4½ gr. (0.3 g.) of epanutin), there was an increase of fits compared with the combination of drugs or of phenobarbitone alone in the doses prior to reduction.

Patients Previously on Epanutin

Unfortunately only six patients who had previously been on epanutin for over a year were available, and these now also had 1 gr. (65 mg.) of phenobarbitone twice a day, after food. As this produced no effect on the frequency of fits or on the behaviour of the patients, at the end of three months the dosage was in each case increased to 1 gr. three times a day and continued for a period of six months, at the end of which time the phenobarbitone was withdrawn, the patient thus being put back on epanutin alone.

The results of this step were as follows. Two patients who had had their fits well controlled by epanutin alone did not experience further improvement on the addition of phenobarbitone, either in frequency of fits or in quality of behaviour. Two cases not so well controlled by epanutin showed no improvement when the two drugs were combined. In the fifth case there was a marked reduction of fits and an improvement in behaviour, due apparently to the combined action of the two drugs. The sixth patient developed toxicity in the form of dullness, apathy and general lethargy, and wretchedness, which cleared up when phenobarbitone was omitted. In the fifth case withdrawal of epanutin led to a return of frequency of fits and quality of behaviour to their previous levels.

Use of Epanutin and Phenobarbitone Combined in Capsule Form

One of the chief drawbacks to the combined method was the numerous doses of medicine required (e.g., epanutin three times a day before meals, and phenobarbitone three times a day after meals). It was therefore decided to try the administration of these drugs together. Capsules were made up containing 1¼ gr. (0.1 g.) of epanutin and 3/4 gr. (50 mg.) of phenobarbitone, and the following clinical trial was carried out on two different groups of patients.

Eighteen female patients of the type previously described (part of the group of 30 chronic patients), already on epanutin 1½ gr. thrice daily and phenobarbitone 1 gr. thrice daily, were put on to one E and P capsule three times a day immediately after meals, and the other drugs were withdrawn. In the absence of any contraindications this medication was in each case continued for eight weeks. The five of the eighteen patients whose fits had been diminished on epanutin capsules and phenobarbitone tablets separately had them equally well controlled following the administration of the combined drugs in capsule form, and in nine of those cases where the fits had been unchanged on epanutin and phenobarbitone separately they remained similarly unchanged in frequency on the E and P capsules. In the four remaining cases no untoward occurrence took place until they had been on the capsules of the combined drugs for a number of weeks, when they each had a batch of several fits in the course of a few days. It is probable that the increase in the number of fits was associated with a reduction in the total dose of phenobarbitone involved in changing to the E and P capsules.

There was no digestive upset of any kind, but one patient who had been on E and P capsules for a month had four severe fits and for a few hours ran a temperature of 100.2° F. (37.9° C.). This woman had always been subject to fits in batches, so that the occurrence of these and the concomitant temperature could obviously not be proved to be the result of any change in medication. Nevertheless, it was thought advisable to discontinue the E and P capsules. Another patient who had developed a typical ataxia and confusion on epanutin and phenobarbitone separately was among those tried on the combined drugs, and she soon developed similar toxic symptoms.

Fifteen suitable male patients were also tried on one E and P capsule thrice daily, and during the three weeks they were on these capsules no toxic manifestation whatsoever was observed in any of them. The period was too short for any conclusions concerning frequency of fits.

Conclusions

1. *Frequency of Fits and Improvement in Behaviour.*—In five (16.6%) of the 30 cases treated by the addition of epanutin to phenobarbitone there was a marked reduction in the number of fits, and in eight (22%) a definite and consistent improvement occurred in behaviour. The decrease in frequency of fits and the simultaneous improvement of behaviour in only one of the six cases treated with the combination of the two drugs (as opposed to epanutin alone) also represents a percentage of 16.6. The figures of certain authors (Pratt, 1939; Williams, 1939) support these percentages, and some claim higher percentages (Pullar Strecker, 1945). Others (Butter, 1940) have formed lower estimations but do not deny that in certain cases the combination of these drugs is the most effective form of therapy that can be administered.

2. *Toxicity.*—(*a*) Of the 30 cases in which epanutin was added to previous phenobarbitone medication only one showed toxicity (in the form of ataxia) when it was added in doses of 1½ gr. twice a day, but a further five developed various toxic nervous symptoms when the dose was increased to 1½ gr. thrice a day, and in every case the symptoms cleared up after epanutin was withdrawn. From a survey of the literature (Blair, 1940) it is plain that the toxic symptoms were similar to those which may be experienced when epanutin is given alone, and it seems definite that the combination of epanutin with phenobarbitone does not add to its toxicity. Thus the more severe manifestations seen when epanutin is given in 4 or more capsules per day

* The term "fits" in this paper refers to major epileptic fits only.

(=6 gr., or 0.4 g., total) were not observed. (*b*) Of the six patients previously on epanutin one developed toxic symptoms. She became dull, retarded, lacking in powers of concentration, devoid of energy, and generally miserable, and on withholding the phenobarbitone these symptoms cleared up. The symptoms are those that might be expected from phenobarbitone alone (Blair, 1940), and again it seems that the combination with epanutin does not produce increased toxicity. (*c*) Only one of the 18 female cases and none of the 15 males treated with E and P capsules showed any toxic symptoms during the time they were on this therapy (over 5,000 capsules were used in all). It is interesting to note that Pullar-Strecker (1945) maintains that the drugs given in combination (in E and P capsules) are less toxic than when given alone. This has not yet been established, but the present work does seem to show that they are at least not more toxic in combination than separately.

3. *Dosage.*—It is obvious from the foregoing that the addition of 1½ gr. of epanutin twice a day to those patients previously on phenobarbitone produced no effect on the incidence of their fits, but when the dosage was increased to 1½ gr. three times daily better results were obtained. Similarly the addition of phenobarbitone, 1 gr. (0.65 mg.) twice daily, to patients previously on epanutin produced no noticeable effect, but when the dose was increased to 1 gr. thrice daily it caused a marked decrease in the number of fits and an improvement in behaviour in one of these six cases. The number of cases in the present series was of course too small to offer any definite conclusions. Nevertheless, from my experience of other cases I have found that the dosage in which epanutin is most frequently used with success is 1½ gr. three times a day (Blair, 1940), and similarly the dosage of phenobarbitone most often used in this type of case is 3 gr. (0.2 g.) daily. However, in view of the fact that the cases dealt with here were confirmed psychotics, it was thought that for general use a more suitable dose of phenobarbitone would be 3/4 gr. (0.05 g.) thrice daily. I therefore wondered if capsules containing both drugs could be made up in these doses, and consulted Parke, Davis and Co. regarding such a possibility. After pharmaceutical investigation they reported favourably and produced the E and P capsules for trial. Since 1941 the capsules have been on the market and been used quite extensively. Pullar-Strecker (1945) described very good results from their use and stated that he now uses them exclusively in place of epanutin alone.

It is to be noted that a few patients showed an increase of fits after being on these capsules for a few weeks. This was probably associated with a reduction in the total dose of phenobarbitone in capsule form as opposed to the previous dose when given alone. In such cases it may be necessary to administer phenobarbitone alone once or twice daily to increase the total dose to the original value.

Pharmacology

Unfortunately, comparatively little is known of the exact mode in which phenobarbitone and epanutin achieve their anticonvulsant effects. The principal seat of action of phenobarbitone is probably the diencephalon, but it is thought that it also affects the cortex and thus produces its hypnotic action. In therapeutic doses it has been recovered from the above areas only, whereas in large doses it may be found in every part of the nervous system in equal amounts (Keeser and Keeser, 1928).

The exact site of action of epanutin is unknown, although it is probable that it acts differently from phenobarbitone. In large doses it has a depressant effect on the whole central nervous system. It differs from phenobarbitone in chemical composition, hydrogen-ion concentration, and anticonvulsant effect on electrically produced convulsions in animals; it has a greater anticonvulsant effect than phenobarbitone (on certain patients) and a greater toxicity; and there is an absence of hypnotic effects. It has been suggested that epanutin may produce its effect by (*a*) alteration of permeability of the cortical cells (Putnam and Merritt, 1941), (*b*) some metabolic effect (Hemphill and Walter, 1941), or (*c*) raising the electrical threshold of the cortical cells (Naffziger *et al.*, 1942). Observations made on the differing effects of epanutin and phenobarbitone in inhibiting convulsions produced by cardiazol (leptazol) (Blair, 1940; Frost, 1939) may also indicate different modes of pharmacological action. Taking everything into consideration it may at least be said that epanutin almost certainly has a completely different anticonvulsant effect from that of phenobarbitone (Blair, 1940; Williams, 1939; Putnam and Merritt, 1941).

Synergistic action of these drugs has been claimed by Cohen *et al.* (1940). In my opinion the present work indicates that the fundamental difference in the modes of action of these drugs persists when they are used in combination—that is to say, the one drug does not reinforce the other, but two entirely different effects are present instead of one. This is shown by the fact that the beneficial effect of the second drug is not obtained unless it is given in sufficiently high doses to produce an effect in itself. For instance, the addition of one or even two capsules (1½–3 gr.) of epanutin produced no beneficial effect, and I have shown previously (Blair, 1940) that these doses are very seldom effective in this type of case. It is only when epanutin is given in three capsules (4½ gr.) that some cases benefit. Again, some cases on 3 or 4 gr. (0.2 or 0.26 g.) of phenobarbitone, to which had been added 4½ gr. (0.3 g.) of epanutin daily, later had the phenobarbitone reduced to 2 gr. (0.13 g.). In four such cases reduction of the phenobarbitone led to an increase in fits. All these observations indicate that epanutin did not replace the phenobarbitone. This was further instanced in the cases placed on E and P capsules exclusively. In a few cases a batch of fits occurred several weeks later, and, as I have already pointed out, this was probably due to the reduction of the total dosage of phenobarbitone involved. I was not able to observe these cases long enough to see the effect of adding phenobarbitone to restore the original level. It is to be noted that in not a single case did combination of the drugs produce an increase in fits. Also, the toxic effects of one drug are apparently neither diminished nor enhanced by the second drug.

Epanutin is soluble in water and has a reaction in solution of about *p*H 11.7. Phenobarbitone is practically insoluble in water, but in suspension gives a reaction of approximately *p*H 5.6. When the two compounds are mixed in a capsule the effective reaction in solution is essentially that of the dissolved epanutin, and is again approximately 11.7. This admixture in capsules (E and P capsules) appears from the present work to be a convenient and innocuous means of administering them together, despite its marked alkalinity.

Summary

Several previous articles have claimed a synergistic action between phenobarbitone and epanutin. The present investigation confirms that this synergism exists in not less than 16% of cases.

It is indicated that when the drugs are used in combination the toxicity of one is neither enhanced nor diminished by the presence of the other.

Knowledge of the pharmacological action of these drugs is still sparse, but it is here shown that they probably produce their anticonvulsant effects in entirely different ways, and that used in combination they act by summation of two different processes.

It is considered that the optimum dosage for combining these drugs is 1½ gr. (0.1 g.) of epanutin to 3/4 gr. (0.5 mg.) of phenobarbitone.

Capsules ("E and P") containing these doses were given a successful initial trial. The capsules have now been placed on the market and very good results have been reported from their use (Pullar-Strecker, 1945).

I have to thank Dr. G. Lilly, medical superintendent of Cane Hill Hospital (where these researches were made) for his interest and encouragement in carrying out this work, and Messrs. Parke, Davis and Co. for their co-operation in producing the E and P capsules.

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NOMOGRAMS FOR RELATIVE HUMIDITY

BY

G. H. BELL, M.D., B.Sc.

AND

J. B. de V. WEIR, M.A., M.B., B.Sc.

(From the Institute of Physiology, Glasgow University)

Wynne (1947) has recently given simplified formulae for calculating the relative humidity and drying capacity of the atmosphere. These values can be read off direct on the accompanying nomograms and no calculation is required. A stretched black thread or a ruler placed so as to lie on the readings of the wet-bulb and dry-bulb thermometers cuts the third scale (relative humidity or saturation deficiency) at the required value.

The basic formula is $P = S^w - f\triangle$, where P is the partial pressure of water vapour in the air (in millibars), S^w the saturated water-vapour pressure at the temperature of the wet bulb, f a constant depending on the barometric pressure and the velocity of the air, and $\triangle$ the difference in Fahrenheit readings between the two thermometers. The relative humidity H is given by $H = 100\frac{P}{Sd}$, where Sd is the saturated water-vapour pressure at the temperature of the dry bulb, and the drying capacity or saturation deficiency of the air in millibars by $Sd - P$. The charts are based on the exact values of the partial pressure of water vapour under saturated conditions, and have the additional advantage that both Fahrenheit and Centigrade scales have been incorporated. The nomograms are designed for use in calm conditions such as exist in buildings where f can be taken as 0.5. They do not apply accurately to observations made in the Stevenson screen or with the sling psychrometer where the value of f is lower.

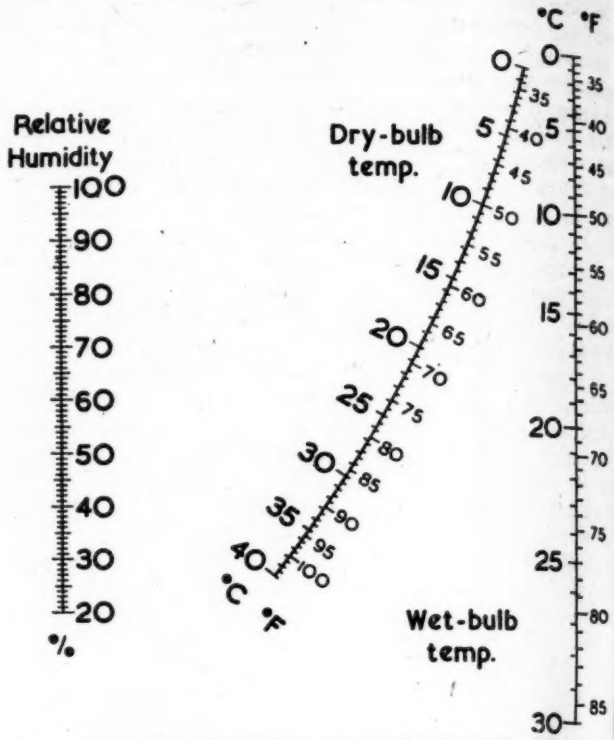

FIG. 1.—Nomogram for finding the relative humidity of the air from the dry-bulb and wet-bulb temperatures.

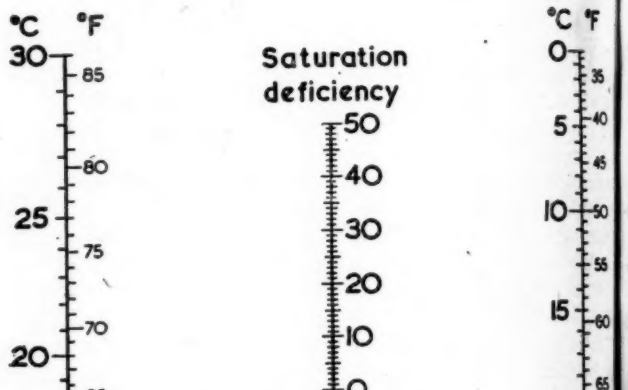

FIG. 2.—Nomogram for finding the drying capacity or saturation deficiency of the air from the dry-bulb and wet-bulb temperatures.

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Medical Memoranda

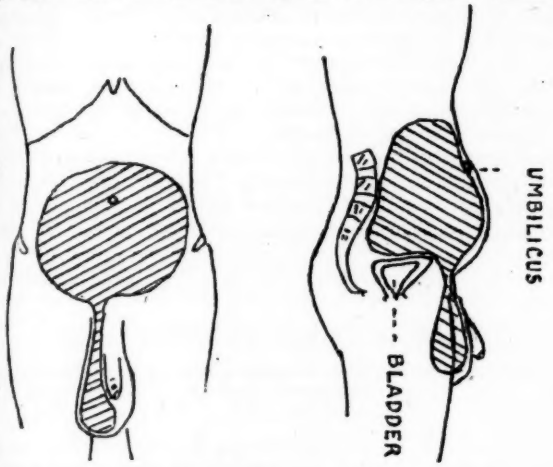
Enormous Intra-abdominal Hydrocele

In the Lango district of Uganda hydroceles are common and reach very much larger dimensions than at home. In this station hospital we operate on six to eight a week, averaging 1 to 2 pints (0.57 to 1.14 l.) We recently dealt with one of such unusual interest with regard to its anatomical relations rather than its enormous size that it seems worthy of publication.

CASE REPORT

An old African reported at a dispensary because he had had a swelling in the right side of his scrotum for some years (the African in these parts has very vague ideas of time). Examination revealed a right hydrocele of moderate dimensions, estimated at about a pint. It was not quite typical of a hydrocele since it could not be completely flexed on the abdomen, although it was dull on percussion, tense, and obviously contained fluid. This slight divergence from the normal clinical findings was attributed to a much-thickened cord, a common accompaniment to large hydroceles which have been carried for many years.

A much more interesting finding than the hydrocele was a very large abdominal tumour extending out of the pelvis to midway



between the umbilicus and xiphisternum. This gave the appearance of a seven-month pregnancy. It was diagnosed as an enormously distended bladder, although no history of dysuria could be obtained. Histories in these people are so unreliable that they must often be disregarded. A rubber catheter was passed but seemed barely to reach the bladder, and would go no further. Only a few drops of urine were obtained. Rectal examination revealed no enlargement of the prostate. It was decided to operate on his hydrocele and follow this by the passage of sounds, and if this should prove unsuccessful a suprapubic cystotomy was anticipated.

Under spinal anaesthesia the tunica vaginalis was exposed through a low inguinal incision. The hydrocele was tapped before delivery, and during the evacuation of six pints (3.41 l.) of the usual straw-coloured fluid the abdominal tumour was observed to subside. After opening the sac an exploring finger could be freely moved throughout the lower abdomen and pelvis. The wall of the sac lay above and in contact with the bladder, a sound being passed to ascertain the exact relationship. It was in contact with both sides of the pelvis and the promontory of the sacrum. It reached upwards as far as a large Kocher forceps would reach, though the fundus could be easily brought in contact with the examining finger by pressure on the abdomen above. There was a patch of calcification on the wall about the size of a half-crown.

Although the fundus could be gripped with a forceps and the sac partially everted, it was not possible to strip it off the adjacent structures. The scrotal end of the sac was left open with the edges everted in the hope that re-formed fluid might drain into the scrotal tissues and be absorbed. Eleven days after the initial operation 1 pint (0.57 l.) of blood-stained fluid was evacuated through a suprapubic incision. The patient was discharged from hospital on the 21st day with no further evidence of the fluid again collecting.

COMMENT

How this hydrocele sac formed is a matter of speculation. Presumably the processus vaginalis had been obliterated high up, and the upper end of the tunica vaginalis grew intra-abdominally in response to the pressure on the fluid collecting within it, in a somewhat similar manner to the hypertrophy of the tunica within the scrotum in normal hydroceles. The proportions and relations of the hydrocele can be seen from the accompanying diagrams.

Our thanks are due to the Director of Medical Services, Uganda, for permission to publish this case.

D. P. BURKITT, M.D., F.R.C.S.Ed.
B. N. KUNUNKA.

Convulsions under Thiopentone

The following case report seems to be interesting enough to merit publication.

CASE REPORT

A workman aged 50 was admitted to hospital on March 1, 1947, suffering from a laceration of the right leg. His physical condition was fair. He was given 1/4 gr. (16 mg.) of morphine sulphate and 1/100 gr. (0.65 mg.) of atropine sulphate at 12.30 p.m. At 2 p.m. he was taken to the theatre for operation. One gramme of thiopentone ("pentothal"—Abbott laboratories) from a recent stock in regular use was prepared as a 5% solution. One of us (A.F.) administered this intravenously in the left ante-cubital fossa; 0.5 g. was used for induction, and as the operation site was prepared a further 0.25 g. was given slowly. About three minutes after starting the anaesthetic and soon after the surgeon had begun the débridement of the wound the left forearm began to move convulsively with a pronating movement; this was followed by movements of the legs, and fibrillary twitchings were noticed in the exposed muscle. Although the patient was already deeply anaesthetized and did not respond to the eyelash or eyelid reflexes, a further 0.25 g. (making a total of 1 g. in all) was given in an attempt to stop the convulsions and continue the operation. The movements, however, increased and spread to the diaphragm, the rapid convulsions of which could be seen in the epigastrium. The jaw was tightly closed and the chest rigid. The patient became cyanotic, and an oral airway was passed with the help of a mouth gag. Oxygen was administered by pressure on the reservoir bag and 1.7 ml. of nikethamide was given intravenously. Soon afterwards the patient began to vomit a lot of thick brown mucus without effort. There was no laryngeal spasm or coughing. No convulsive movements were seen in the face, but the pupils were dilated to about two-thirds the diameter of the cornea—probably an effect of anoxia. The patient was returned to the ward, the convulsions continuing. By 2.40 p.m. the convulsive movements were wearing off, but he was still vomiting. His blood pressure was 110/75, the pulse 100, and the general condition not bad. He was taken back to the theatre still unconscious, and the operation was completed uneventfully in about half an hour under oxygen and a little ether.

The following findings were made immediately after the operation: Blood urea, 18 mg. per 100 ml.; urine urea, 2.4 mg. per 100 ml.; routine urine examination, neutral; specific gravity, 1020; albumin and sugar, nil; blood sugar, 95 mg. per 100 ml.; Wassermann reaction, negative; fundi, no significant changes. On questioning the patient the following day he was found to be an opium addict, smoking about 4 g. daily.

DISCUSSION

This was not a case of laryngeal spasm, often associated with thiopentone administration; nor was it simply a tremor which is sometimes seen on induction with this drug. The movements were definitely convulsive and interfered with respiration. It was quite unlike a true "ether" or "anaesthetic" convulsion, which usually starts with twitching in the orbicularis oris muscle: in this case the face was not affected at all. The patient had a temperature of 97.6° F. (36.4° C.); the theatre temperature was moderate. Only a small dose of atropine was given pre-operatively. There was no anoxia up to the time the convulsions started. In any case thiopentone is an effective antidote to "anaesthetic" convulsions. The association with opium addiction may be significant, but the amount smoked daily was small. Many addicts have been anaesthetized with thiopentone in this hospital, but this is the first case of convulsions seen here.

We wish to thank the chief medical officer of the Anglo-Iranian Oil Company, who has kindly consented to the publication of this note.

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Reviews

ANAESTHESIA

The Chemistry of Anaesthesia. By John Adriani, M.D. (Pp. 530; illustrated. 35s.) Oxford: Blackwell Scientific Publications. 1946.

The author of this book, an American anaesthetist who has published numerous papers on the chemistry of anaesthetics, is well qualified to write this expansion of his teaching syllabus for postgraduate students. The scope of the book is much wider than might be expected from its title, for the author considers such subjects as the liquefaction of gases, the role of acetylcholine in the nervous system, and the effects of anaesthetics on liver function. In Part I he discusses the laws governing the behaviour of gases and applies them to such practical problems as the storage of anaesthetic gases in cylinders, types of flowmeters, methods of gas analysis, and the physicochemical basis of air embolism. He gives a full account of the absorption of carbon dioxide by soda-lime in closed-circuit anaesthesia—a subject to which he has made original contributions. In Part II, after some introductory remarks on the main groups of organic compounds, he discusses hydrocarbons, alcohols, ethers, alkaloids, barbiturates, and other drugs. Various tables permit a quick survey of some large groups of these compounds. In addition to a description of the chemical properties of each anaesthetic and its method of manufacture he gives information on its concentration in the blood, its detoxification in the body, and tests for purity. There are chapters on local anaesthetics, atropine, and analeptics, and a survey of anaesthetic explosions and their prevention. In Part III, on the physiological and biochemical aspects of anaesthesia, he begins by reviewing various theories of the mechanism of narcosis, and then discusses the effects of anaesthetics on the composition of body fluids, describing in detail the influence on the acid–base equilibrium. Other chapters deal with the effects of anaesthetics on liver function, formation of urine, vitamins, and cell oxidation. He gives some interesting information on the rather neglected problem of elimination of anaesthetic drugs; however, here as in various chapters of Part I and II factual errors occur.

The value of the book is enhanced by over forty pages of classified bibliography, a short glossary, and a detailed subject index. It is well printed and almost free from errors. One minor omission is the absence of trichlorethylene from the index. The work is somewhat too bulky as a textbook for the general anaesthetist, and not sufficiently comprehensive as a reference book for a research department. Omission of various paragraphs of little importance in Parts II and III (e.g., pp. 405, 501–3) would make room for more factual information on, for example, methods of analysis and solubility of anaesthetics in body fluids. Readers would also appreciate being told occasionally which of several numerical results is the more reliable in the author's opinion.

H. G. EPSTEIN.

URGENT SURGERY

Urgent Surgery. Volume I. Edited by Julius L. Spivack, M.D., LL.D. (Pp. 714; 244 figures having 572 illustrations (14 illustrations in colour). $10.50.) Springfield, Illinois: Charles C. Thomas.

This, the first volume of a work on urgent surgery, is clearly printed, well produced, and copiously illustrated; all the sections are well written by experts and the information is up to date and readily accessible through a good index. Apart from a few preliminary chapters on general subjects such as shock, haemorrhage, anaesthesia, and infections, this volume is wholly concerned with abdominal surgery. The sections dealing with the liver and bile-ducts, appendicitis, and intestinal obstruction merit special praise, though it might have been better to include strangulated hernia in the latter section. Nevertheless the work needs some alterations and additions if it is to be of use to the practical and perhaps inexperienced surgeon. The editor states that he rejected the term "emergency surgery," which implied the necessity to intervene surgically within minutes or hours, and adopted the title "urgent surgery," under which (in his opinion) are included cases in which operation becomes imperative "within a few days, if life or health is to be preserved." This definition is interpreted very widely, many would say much too widely, for it leads to the inclusion of fully illustrated accounts of the operations of gastrectomy, gastrostomy, gastro-jejunostomy, splenopexy, and even abdomino-perineal excision of the rectum.

Some very rare conditions are fully described, while other more common and very important conditions are not sufficiently emphasized. The discussion of acute dilatation of the stomach occupies less than two pages, but six are allotted to volvulus of the stomach. Eight pages, in which five different techniques are described, are devoted to the rarely performed operation of splenopexy, while the treatment of sigmoid volvulus is described in only seven lines. On several important points the advice given is not definite enough; for example in the section on urgent surgery of the colon we are advised that for resection of the left colon we may use (if the multiple-stage method is adopted) either the Mikulicz or the Rankin technique, but no preference is given. Moreover, it is astonishing to be told the old method of waiting a few days before cutting away the exteriorized gut in a Mikulicz operation; Paul's practice of cutting away the gut at the primary operation has been the common technique for many years. There are some conflicting views expressed in different parts of the book. On p. 476 we read that lack of rigidity with shock and abdominal pain are particularly characteristic of occlusion of the mesenteric vessels, while on p. 616 rigidity is stated to be present in 45% of such cases. On p. 52 the statement is made that suture of ruptured liver is rarely possible and usually increases the bleeding, but later in the book we find several pages (quite rightly) devoted to methods of suture of the liver.

One other small point of criticism: we are recommended to use hypodermoclysis or venoclysis for introducing fluids into the body, but neither in the index nor in the text did we find a single reference to the valuable and safe method of proctoclysis.

V. ZACHARY COPE.

HORMONES IN GYNAECOLOGY

Diagnostic Hormonal et Traitements Hormonaux en Gynécologie. By Claude Béclère. Preface by Prof. H. Simonnet. (Pp. 372. 525 francs.) Paris: Masson et Cie. 1946.

"Ce livre n'est pas une compilation bibliographique; ce n'est pas non plus l'analyse actuelle de l'expérimentation chez l'animal, c'est avant tout un travail de clinique et de pratique médicale." So writes Prof. H. Simonnet in the preface. It is indeed a résumé of the author's views and methods derived from his own clinical experience. He gives a short and orthodox account of the physiology of the female genital apparatus and of the chief actions and uses of various hormones. In the main section he discusses the diagnosis and treatment of functional disorders as they occur in four periods of life: (*a*) puberty and adolescence, (*b*) maturity, (*c*) pre-menopause, (*d*) post-menopause. For describing management and treatment this arrangement has advantages, but it involves a good deal of repetition.

Since the author's statements remain, for the most part, unqualified by references to the literature and to contrary opinions, many readers will be critical of certain details. For instance, few will agree that spasmodic dysmenorrhoea is due to "hyperfolliculinism" and that it is usually benefited by progesterone therapy; that all cases of pre-menopausal haemorrhage are "hyperhormonal" and associated with endometrial hyperplasia; that hysterosalpingography can replace diagnostic curettage for the purpose of excluding carcinoma corporis uteri; that delayed puberty is sometimes due to a hyperhormonal state; or that over-activity of the pituitary plays an important part in most cases of endocrine obesity. Though it has its faults this book nevertheless has its attractive features. The author lays stress on diagnosing before treating and on the necessity not only for determining the nature of the dysfunction but for excluding an occult organic cause of symptoms. In this respect the value of hysterosalpingography is properly stated. "Le diagnostic organo-hormonal" which Béclère describes appears to consist in a careful assessment of the development of secondary sex characters as a measure of the degree and type of endocrine disorder, and is therefore hardly original. He recognizes the

importance of the constitutional factor in the aetiology of menstrual disturbances when discussing amenorrhoea and haemorrhage of "congenital" origin. Of interest is the very small dose of oestrogens that he advises for the treatment of amenorrhoea—1 to 5 mg., often in a single injection, in one month. In contrast he advocates implantation of a tablet of as much as 200 mg. of testosterone for puberty haemorrhage. He covers the field of sex endocrinology fairly well, if somewhat thinly in places.

The book is useful for its practical approach, and if Béclère's views are not all acceptable, they nevertheless merit the attention of those interested "à cette extraordinaire physiologie hormonale de la femme."

T. N. A. JEFFCOATE.

HYPERTENSION

Renal Hypertension. By E. Braun-Menéndez, J. C. Fasciolo, L. F. Leloir, J. M. Muñoz, and A. C. Taquini. Translated by Lewis Dexter, M.D. (Pp. 451. $6.75.) Springfield, Illinois: Charles C. Thomas. 1946.

Those acquainted with the first edition of this book, published in Spanish in 1943, will welcome this translation into English by a man whose own contributions to the subject are considerable and whose previous collaboration with the workers of the Buenos Aires school so well qualifies him for the task. The volume is a tribute to the painstaking efforts of the South American authors, who acknowledge in their introduction the inspiration and continued help of Prof. B. A. Houssay. Those approaching the subject for the first time will find here all the information available, and those who, in England and America, are working in this field will find this an invaluable book.

Dr. Dexter has wisely sought not to produce a line-by-line translation of the Spanish edition but rather to present the authors' views in English, and he has therefore included advances made since 1943. The first eleven chapters are concerned with the production of experimental hypertension in animals, the techniques used, and the mechanism of production and the properties of renin, hypertensin, hypertensinogen, and hypertensinase. The secretion of renin, the protective action of the normal kidney, the modifying influences of the endocrine glands, and the effect of pregnancy on experimental hypertension are fully discussed before the properties of certain other vasoconstrictor bodies are described. The following six chapters are devoted to hypertension in man, its classification, the mechanism of its production, and especially its relation to renal ischaemia and renal disease. Two chapters cover the treatment of human hypertension, the one its medical and the other its surgical treatment; and a final chapter deals with the relation between hypertension in man and experimental hypertension in animals. An appendix gives in detail the methods used in Buenos Aires for the assay of renin, hypertensin, hypertensinogen, and hypertensinase. The book contains 1,238 references, 93 figures, and an admirable index.

While there will be some who cannot agree with all the authors' interpretation of the facts, no one will deny this book its place as the most complete account of the subject there is, and they will be grateful to Dr. Dexter for making such a work available in English.

HAROLD SCARBOROUGH.

The second edition of I. S. Tassman's *The Eye Manifestations of Internal Diseases* (London: Henry Kimpton; 50s.) has been enlarged by the inclusion of descriptions of ocular allergy, epidemic kerato-conjunctivitis, Hurler's disease, osteopetrosis, lymphogranuloma venereum, toxoplasmic encephalomyelitis, Bowen's disease of the cornea, and Purtscher's disease. The test is rather elementary, though the illustrations are helpful.

Rezeptierkunde, by Prof. T. Gordonoff (Medizinischer Verlag Hans Huber, Berne; Swiss francs 7.50), is a reference book in German for pharmacists, describing the correct way of making out prescriptions, the usual abbreviations, and normal doses of drugs. It describes the preparation of pills, tablets, capsules, suppositories, electuaries, ointments, mixtures, tinctures, emulsions, and solutions for injection, etc. The author considers only the more common drugs of the pharmacopoeia. There is a chapter on prescription errors and incompatibilities, and a list of incompatible drugs. Finally there are notes on "combination therapy" and on synergisms between drugs, and a table of therapeutic and maximum doses.

BOOKS RECEIVED

[Review is not precluded by notice here of books recently received]

Lo Centenario de Pestalozzi. Monografia No. 4 do Boletim do Instituto de António Aurélio da Costa Ferreira. (Pp. 61. No price.) Lisbon. 1946.

A short illustrated historical monograph on Pestalozzi.

Travaux d'Anatomie à la Mémoire du Prof. Fr.-J. Rainer. Bucharest: Imprimeria Nationala. 1947.

Various papers on comparative anatomy (in French) from the University of Bucharest.

What is Atomic Energy? By K. Mendelssohn, M.A., Ph.D., F.Inst.P. (Pp. 180. 6s.) London: Sigma Books. 1947.

Surveys the subject of atomic physics for the lay reader.

Thorpe's Dictionary of Applied Chemistry. 4th ed. Vol. VIII. (Pp. 679. 80s.) Longmans, Green and Co. 1947.

This volume includes from "Methal" to "Oils, essential."

Bone and Bones: Fundamentals of Bone Biology. By J. P. Weinemann, M.D., and H. Sicher, M.D. (Pp. 464. 50s.) London: Henry Kimpton. 1947.

The physiology and comparative anatomy of bones, processes of inflammation and healing, the influence of hormones and vitamins, and an account of skeletal tumours.

Mental Mischief and Emotional Conflicts. By William S. Sadler, M.D., F.A.P.A. (Pp. 396. 30s.) London: Henry Kimpton. 1947.

Psychiatry for the layman.

Textbook of Physiology. By W. D. Zoethout, Ph.D., and W. W. Tuttle, Ph.D. 9th ed. (Pp. 723. 25s.) London: Henry Kimpton. 1947.

New topics discussed include fibrin foam, the rhesus factor, blood grouping, and folic acid.

Man Against Pain. By H. R. Raper. (Pp. 236. 10s. 6d.) London: Victor Gollancz. 1947.

A short illustrated history of anaesthesia.

The Yearbook of Psychoanalysis. Vol. II. 1946 (Pp. 280. 30s.) London: Imago Publishing Co. 1946.

Includes articles on the psychology of punishment, war and peace, and the role of drugs, and an old essay by Freud on Dostoievsky.

Animal Genetics and Medicine. By Hans Grüneberg, Ph.D., M.D. (Pp. 296. 21s.) London: Hamish Hamilton. 1947.

An account of inherited disorders in animals intended primarily for the medical man.

Aids to Qualitative Inorganic Analysis. By R. G. Austin, B.Sc., F.R.I.C., F.R.M.S. 2nd ed. (Pp. 207. 5s.) London: Baillière, Tindall and Cox. 1947.

For medical students taking intermediate science examinations.

Tratamiento Quirurgico del Cáncer de la Vejiga Urinaria. By S. Gil Vernet. Published in *Medicina Clinica*, Barcelona. 1946.

A profusely illustrated monograph on the surgical treatment of cancer of the bladder.

Treatment of the Patient Past Fifty. By Ernst P. Boas, M.D. 3rd ed. (Pp. 479. 27s. 6d. approx.) London: H. K. Lewis. 1947.

Intended as a simple guide for the practitioner on the handling of elderly patients.

Searchlight on Hambledon. By John Dellbridge. (Pp. 160. 8s. 6d.) London: Hurst and Blackett. 1947.

The author of this thriller is said to have known 75 murderers, some of them intimately.

English-Spanish Chemical and Medical Dictionary. By Morris Goldberg. (Pp. 692. 50s.) London: McGraw-Hill Book Company. 1947.

More than 40,000 Spanish translations of English medical and chemical terms.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY AUGUST 2 1947

THE A.R.M. AND THE ACT

There was little that might be described as exciting or provocative on the Agenda of the Annual Representative Meeting which met last week at B.M.A. House from July 22–24, under the chairmanship of Dr. J. B. Miller. Although he told the Meeting at the beginning that the Agenda was not heavy the presence of 340 representatives made it inevitable that the proceedings would not draw to an early close. The man who came with his speech prepared was determined to have his say. Although no dramatic resolutions were passed the Meeting as usual afforded a valuable opportunity for everyone to hear what was the state of medical opinion throughout the country on various matters of significance to those engaged in the arduous task of the daily practice of medicine. It soon became clear that medical men, and especially those in general practice, are on the whole uneasy about the present medico-political situation and the state of the negotiations with the Ministry of Health. On the first day Dr. H. Guy Dain, the Chairman of Council, made a short but concise statement on the discussions that have so far taken place between the Negotiating Committee and its various subcommittees and the officials of the Ministry of Health. He reminded the Meeting that the Minister had agreed to enter into discussions and had agreed, too, that the possibility of fresh legislation should not be ruled out. The Minister himself had used the words "amendment of the Act" as being a possibility arising out of the discussions. Comprehensive discussions had been conducted by subcommittees on specialists and consultants, hospital service, general practice, public health, superannuation, ophthalmic services, and mental services. There had been no attempt on the part of the Ministry's officers to limit the scope of these discussions. "We have stuck to our principles," Dr. Dain said, "and have put forward arguments in favour of them as vigorously as we can. We have not made concessions or retreated at any point from the position we had taken up." Their job had been, he went on, to see that the views of the Representative Body were maintained, and the discussions had materially strengthened the Negotiating Committee in "our own convictions as to the objections we originally put forward." He assured the Meeting that they need entertain no fear that they had been led into discussions which involved acceptance of things of which the Meeting would not approve. As yet there had been no negotiations or discussions with the Minister himself, and Dr. Dain said that they were now preparing a written statement of the arguments put to the Ministry so that this statement could be placed before the Minister at the same time as he received a report from his own officers. When the report has been put to the Minister it is proposed to ask him personally to talk with certain of the subcommittees, so that he may be fully informed of the point of view of the profession. "We shall then expect him," Dr. Dain said, "to produce an amending Bill before the service starts. When we are able to publish the arguments, as we cannot very well do until we have his reply, a meeting of the Representative Body will be called to decide on the attitude of the profession."

Dr. Dain pleaded that the Meeting should exercise still further the patience they had already displayed, and asked for the trust of the Meeting until the awaited report could be made. The speeches that followed his statement showed that very many members were disquieted about the present situation. They felt that they should have further detailed information and that they should have it now. They were apprehensive lest commitments were being entered into of which the profession would subsequently disapprove. Dr. R. Hale-White, Marylebone, observed that members in the country were puzzled "by this paucity of information." Dr. H. H. Goodman, Newcastle-upon-Tyne, expressed "uneasiness as to what was going on behind closed doors," and complained that for six months the profession had not known where it stood. Uneasiness at the secrecy which had surrounded the negotiations was also expressed by Dr. J. Ewart Purves, Bromley. He made a plea for open diplomacy. As a member of the Negotiating Committee, Dr. R. W. Cockshut was able to tell the Meeting that the Negotiating Committee had given nothing away. In fact, throughout the discussions it had seemed to him as a critical and mainly silent member that the Committee had grown in strength.

Negotiations on such an important issue as the National Health Service Act must obviously have occupied much time, and the Meeting was perhaps a little unappreciative of the hard work done on its behalf by the many men serving on the various subcommittees during recent months. This work has demanded close attention to detail and has been carried out at much personal sacrifice to those who had to take time off from their professional life in order to see that the case for the medical profession was adequately and forcefully presented. It would seem to be a step of doubtful wisdom to break into the middle of negotiations with premature publication of the course of the discussions that have already taken place. The profession has appointed its own Negotiating Committee, and it is surely not too much to ask that the profession should trust it to see the business through to the end. But at least the anxiety on this matter displayed at the Annual Representative Meeting will show the Minister of Health that those who will have to do the work in the new Health Service he has created still remain deeply disturbed by many features of the Act and will not be willing partners with him in it until the causes of discontent are removed. The Negotiating Committee itself will—if that be necessary—feel still further strengthened in its resolve to press matters to their final conclusion and not to yield on matters which it considers fundamental.

The course of action for the immediate future is now plain. The Minister will receive the statement drawn up by the Negotiating Committee; he will be asked to

receive the Negotiating Committee and certain of its sub-committees, and the profession will then expect him to state how far he is prepared to go in meeting the objections raised to the present Health Act. This having been done, the profession, fully informed of the whole matter, will be asked to vote on it by answering questions sent out on a Plebiscite form. The Council, after being instructed by a Special Representative Meeting, will indicate to members of the B.M.A. what line of action should be taken, and before the end of the winter all these troublesome matters should be settled—and will be settled once and for all if the profession has the necessary loyalty and coherence of action to continue strongly in the direction it decides to take. Without the medical profession behind him the Minister cannot operate the National Health Service Act. This is the one fact that medical men should keep firmly in mind.

BACTERIAL CHEMOTHERAPY

The Eleventh International Congress of Pure and Applied Chemistry, concluded last week, provided a valuable survey of a many-sided research on chemotherapeutic substances. One approach, the most fundamental, is to start with the metabolism of the organism to be attacked and in a planned and logical way to seek to interfere with it. Such work is of a long-term character, but is likely to become increasingly important as the standard set by chance-discovered substances—among which penicillin must be included—is progressively raised. A second approach, which in practice is closely connected with the first, is to take an existing chemotherapeutic agent and to investigate in the laboratory the chemical mechanisms by which its effects on the organism are brought about. Woods's observation that sulphanilamide was antagonized by para-aminobenzoic acid,[1] and his deduction from this, later confirmed,[2] that the latter substance was an essential metabolite for bacteria with which sulphanilamide competed, provided the first and now classic example of this approach.

Gale and Taylor, at Cambridge, have extended this approach to penicillin, and have obtained evidence that its effect—or, at any rate, one of its effects—is to prevent the passage through the cell wall of the glutamic acid needed for the synthesis of proteins within the bacterium. Working with *Staph. aureus* they have found a progressive fall in internal glutamic acid when penicillin is present in the culture medium. During this period the general metabolism of the bacterium appears to be unaffected. There is no change either in respiration or in the rate at which glucose is oxidized. The natural assumption is that the fall in glutamic acid is due to the using up of existing supplies for protein synthesis, and that the only change which has taken place is the cutting off of replacement supplies from outside. It is suggested that this blocking effect takes place at the surface of the cell wall. This is a most remarkable discovery, and the more so as some evidence suggests that resistance to penicillin—other than through direct destruction by the enzyme penicillinase—may be connected with the ability, natural or acquired, of the bacterium to make its own glutamic acid from simpler constituents. There is an obvious temptation to assume further that this mechanism, together with the production of penicillinase by particular strains, will account for all cases of penicillin resistance. But this generalization cannot be substantiated; as Sir Henry Dale pointed out in his congress lecture, printed elsewhere in this issue, it may be unwise to assume in a hurry and on limited evidence that a single such mechanism can be universally applied. This warning has already been proved timely by some observations reported by the same two workers on the operation of the sulphonamide drugs.

It might have been thought that this had been settled once and for all by the investigations of Woods and others. But to the mechanism of competition with para-aminobenzoic acid Gale and Taylor have now added an apparently direct effect on glutamic acid metabolism. Whereas with penicillin there was a gradual falling in the internal concentration of this substance within the bacterium, the effect of sulphonamides was to produce an abnormal accumulation. This is taken to mean that absorption through the cell wall was proceeding as usual, but that utilization within the organism had been blocked. What the connexion, if any, may be with the earlier discovery is not clear. But in this case, as with penicillin, "any hint is of value which gives chemists a rational clue to follow."

If these Cambridge investigations are of more immediate interest, mention must be made also of the attempts reported by the Medical Research Council unit at the Lister Institute to go one stage behind such work and elucidate the method of combination between the normal metabolite and the enzyme of which it is the substrate.[3] As an example, a scheme has been worked out to explain the chemical combination of indole and the tryptophan-synthesizing enzyme of *Salmonella typhi*. Such work has inevitably an air of remoteness and complexity. Yet if the ultimate aim is to monopolize the services of the enzyme by the introduction of alien and competing substances it is reasonable to investigate first the types of chemical combination to which the enzyme is adapted.

A third approach, less purist in conception, is to work out the structure of a natural antibiotic, devise methods of synthesis, and then design in the laboratory a series of chemical variants. Penicillin, as might be expected, has provided the main inspiration, although the first stage has also been completed in the case of streptomycin, and for that matter of a number of further substances the therapeutic use of which is either unlikely or not yet established. Taking penicillin first, Hodgkin, Rogers-Low, Bunn, and Turner-Jones have now contributed the first account—pending the long-awaited monograph on penicillin—of the final settlement of its structure by *x*-ray analysis. This proved a long and laborious undertaking, the penicillin molecule being both unsymmetrical and of unusual form. In the end the position was fixed in three dimensions of every individual atom in sodium and potassium benzylpenicillin, and that with sufficient accuracy to rule out decisively the possibility of any alternative structure. No more difficult investigation of the kind has been

[1] *Brit. J. exp. Path.*, 1940, **21**, 74.
[2] Rubbo, S. D., and Gillespie, J. M., *Nature*, 1940, **146**, 838.
[3] Fildes, P., and Rydon, H. N., *Brit. J. exp. Path.* (in the press).

undertaken, nor is its usefulness reduced by the fact that the same conclusion would in any case have been reached, although with less certainty, by purely chemical means. On the contrary, penicillin is evidently a molecule of quite exceptional interest to the biologist, and, with the suggested cell-wall mechanism in mind, exact knowledge of its physical shape must be no less needed for the full explanation of its action.

The chemical position was not, of course, so clear when this Oxford work was begun. In place of the beta-lactam structure, which is now known to be correct, an alternative and more open structure was generally favoured, and it was on this basis that the Merck laboratories in the United States and Sir Robert Robinson's laboratory in Oxford independently conceived the first synthesis of penicillin.[4] This, as is now generally known, was later carried to the stage of isolation in pure form—though still with a yield of less than one part in a thousand—by du Vigneaud and his team in the United States.[5] This was technically notable, and du Vigneaud now suggests that by perseverance with this approach it should be possible to obtain advance knowledge of the effects of chemical modifications. The investigations reported by Sir Ian Heilbron's team at the Imperial College of Science and Technology have wider possibilities. Working towards the now accepted structure as their target, at least two routes have been designed for the production of substances of the desired type. Not all the stages of synthesis have yet been attempted, and as Dr. A. H. Cook, who summarized progress, was careful to point out, there is many a slip between paper chemistry and the real thing. None the less, considerable progress has been made, and although these synthetic penicillins are unlikely, when produced, to be identical with any of the natural products, they will contain what to the chemist is the same key structure, and it is not unlikely that one or more of them may prove as potent biologically. Hopes that it may prove possible to extend in this way the range of organisms against which penicillin is effective—its "bacterial spectrum" in the current jargon—are unfortunately discouraged by the suggested mode of action. If it is correct that penicillin resistance is conferred by power to make glutamic acid, then no tinkering with the design of penicillin could affect this immunity. Later experimental results with synthetic variants should therefore provide a valuable check on the Cambridge picture, apart from their potential interest to clinical medicine. In the case of streptomycin, there is both less information and more room for improvement. The complete working out of its structure, reported by Folkers, appeared as the outstanding United States contribution on the whole subject. It may also prove of long-term importance—for it is precisely when a substance is imperfect in its operation that the method of chemical variation is most likely to bring reward. Finally, when synthetic penicillins have been achieved, the future will fall to be decided of another piece of terminology which appears ill-conceived. "Antibiotic," if it means anything, should mean a substance which is antagonistic to life. As now employed it means a chemotherapeutic agent derived from a living organism. Is it too much to hope that the production of synthetic penicillins which are not so derived, and which differ but slightly from those produced by the mould, may kill by absurdity a word which means the opposite of what it says and, by its emphasis on origin, suggests a reversion to the witch-doctor conception of organic chemistry?

Last, there is the fourth approach, represented by the search for anti-bacterial substances from among the chemical products of fungi, lichens, algae, actinomyces, fusaria, plants, and bacteria themselves. For the immediate purpose, 99% of such work is likely to prove wasted effort, but it carries always the hope that another penicillin, or even another streptomycin, may be discovered. As Sir Howard Florey emphasized, close and intelligent co-operation between chemists and biologists is needed, and possibly new techniques of investigation, if substances which may prove of therapeutic value are not to be missed in the early stages. From those now under investigation, one only, alliin, can be mentioned which has interest of another kind. Described by Stoll and Seebeck and derived from garlic, it yields a substance after enzyme action which is not only biologically active but also justifies by its existence the esteem in which garlic has long been held in southern Europe as a traditional remedy.

[4] *Science*, 1947, **105**, 653.
[5] Ibid., 1946, **104**, 431.

CONGRESS FOR MICROBIOLOGY

Well over one thousand members took part in the Fourth International Congress for Microbiology, held in Copenhagen during the week ending July 26. The Danes rose magnificently to the occasion, somehow furnishing not only accommodation but every possible amenity for this unexpectedly large number of guests—a greater number than that at any previous congress. Scandinavians, British, and French predominated among the members, but most other European countries and the U.S.A. were well represented: notable absentees were the Germans and Japanese, who were not invited, and the Russians, who were invited but did not come. The scientific business of the congress was divided into nine sections meeting simultaneously in different rooms in the Danish Parliament House; the few general sessions, which included addresses by Bawden on viruses and by Waksman on antibiotics, were held in the somewhat incongruous surroundings of a large theatre. Among the main subjects of direct medical interest in the programme, that of antibiotics and chemotherapy generally was accommodated in much the largest of the available rooms and justified this choice by the very large attendance at some of the meetings. There is a good deal still to be said about penicillin from both theoretical and therapeutic standpoints, and streptomycin received a fair share of attention, including a remarkable paper by Hinshaw which, within the brief time limit imposed on all speakers, surveyed the whole field of streptomycin therapy in tuberculosis, both experimental and clinical. Another noteworthy contribution on this subject was that of Dubos, whose studies of the same disease in mice have produced fundamental information of the sort which makes one wonder why such experiments were not done years ago. Tuberculosis, as much the most important bacterial infection not yet fully amenable to specific treatment, was the subject of other chemotherapeutic investigations; a good deal was also said about its prevention by vaccination with B.C.G. This method is now widely used throughout Scandinavia,

and we have much to learn from what has been done there even during the war and despite the German occupation of Denmark and Norway. Much interest was also aroused by the papers of Albert and Rubbo on the action of 8-hydroxyquinoline, which they have shown to be due to chelation with trace metals in bacteria, in particular cobalt, a substance not previously known to be concerned in bacterial metabolism.

Among filtrable viruses, those of influenza and poliomyelitis received the largest share of attention. There was a note of subdued though unmistakable alarm, which will find a ready echo in this country at the present time, in discussions of the second of these diseases. The parent of fear is ignorance, and we are profoundly ignorant where poliomyelitis is concerned. There is no satisfactory explanation of its geographical distribution and epidemiological behaviour, or of its tendency in recent years to attack higher age groups. One step forward has been the conclusive demonstration of the existence of the virus in flies in an area where infected faeces or sewage was not specially accessible, unless in a flood which had occurred three weeks previously. Epidemiological studies were prominent in the discussion of other infections, making use of the refined typing techniques which have become available in recent times. Those interested in plant diseases, in the bacteriology of dairying, and in industrial fermentation were understood to have passed an interesting time, the latter particularly when entertained at the Carlsberg and Tuborg breweries. The next Congress will be in 1950 in Rio de Janeiro.

A LACTATION VITAMIN

Paprika having already played an honourable part in vitamin history, there is no inherent reason for surprise in the attention paid by Dr. M. El Shahat, of Fouad I University, Cairo, to the oil of the fenugreek herb. Like paprika, it is strongly flavoured, being used in India as an ingredient of curry, and like paprika, Dr. El Shahat reported to the International Congress of Pure and Applied Chemistry, it has yielded a vitamin. The substance in question is stated to have been separated by chromatographic and other means in substantially pure form. It is described as fat-soluble, existing in needle-like crystals with a melting-point of 137° C., and with a characteristic absorption band. Other points bearing on identification are that it is thermostable, not readily oxidized, and contains a single hydroxyl group. Further, it has been differentiated spectrographically, chemically, and biologically from the tocopherols.

Clinical tests at a dosage of 0.125 mg. orally were reported in the same communication. Out of 350 cases of human lactation deficiency, lactation is stated to have been promoted in 345. The volume of milk increased in 158 cases at different stages of lactation by amounts between 160% and 900%, the extent of increase being most marked in the earlier stages of lactation. Of these, 10 had twins and 6 had failed to improve with prolactin or polyvitamin treatment. As regards the quality of the milk, the percentage of fat and the total content of vitamins A, B_1, B_2, and C are stated to have increased. It would seem therefore that the new substance requires further investigation both chemically and under more varied conditions of clinical use. The control of lactation is undoubtedly complex, and it would be unwise to assume in advance that a factor which is of predominant importance under one set of dietetic conditions—as the Egyptian evidence already suggests—is necessarily of equal importance among populations the balance of whose natural foodstuffs is significantly different. It has been provisionally named "H" factor. Although the term vitamin H is seldom used in practice as a synonym for biotin, Dr. El Shahat might well consider before further publication whether a second use of the same letter is desirable.

SWIMMING ON STEAK TEAS

In more spacious days, when only the capacity of the consumer limited the size of a meal, athletes attached importance to what they ate during training and immediately before a contest. Olympic competitors and professional weight-lifters usually had spectacular appetites. University boat crews trained on beef steak and beer. Some unorthodox trainers advocated ice-cream or even bananas as ideal for building up budding record-breakers. The best-developed physique, however, may be of little avail if the time of trial finds the competitor with a full stomach or colon, or else so hungry that he feels exhausted before his ordeal begins. Common sense suggests that it is unwise to indulge in a heavy meal just before an event. So pick-me-ups, varying from a raw egg in port wine to a scientifically adjusted dose of glucose, have been tried to ensure that the individual's performance should not suffer for want of a last ounce of readily available fuel.

A scientific study of this interesting problem, which has an importance transcending athletics, has recently been made by John Haldi and Winfrey Wynn,[1] of Emory University, Georgia. Twelve healthy young volunteers were selected from a naval training unit by their swimming coach, Ed Shea. They were keen "triers" who wanted to improve, but for some time they had failed to make any noticeable day-to-day progress. Under similar conditions, therefore, they could be relied upon to repeat the best performance within their capabilities. The tests were over 100 yd. (91 m.) Each swimmer was timed on five different days after each of four kinds of meals, making twenty swims for each volunteer. The procedure was always the same. At 4.30 p.m. a "heavy" or "light" meal was taken, or a "light" meal supplemented ninety minutes later by 50 or 100 g. of cane sugar. At 7 p.m. the volunteer reported at the pool, and a sample was taken for blood-sugar estimation. He then warmed up by swimming 100 yd. slowly, after which he "toed the mark as in the usual swimming meet, and at a given signal dove into the pool." With Mr. Shea vociferously exhorting him to swim faster, his time for each lap of 33.3 yd. (30.5 m.) was recorded. Then as soon as he had regained his breath another specimen of blood was taken.

The results of the investigation indicated that performances were virtually identical with all four meals. The average time varied little from 75.7 sec., while the rate of fatigue, as indicated by the falling off in speeds in the second and third laps, was the same with each type of meal. The blood glucose, which was about 125 mg. per 100 ml. before and rose to about 142 mg. after the test, was also unaffected by the dietary variations.

Clearly, the exact size of a moderate meal taken at a reasonable interval before strenuous exercise did not seriously affect performance. But very different results might have been found if the conditions had been made more extreme. The "light" meal was equivalent to 551 calories, and it contained 6 oz. (180 g.) of steak—a little less than our weekly meat ration—and half a boiled egg. It was therefore more than a mere snack to a volunteer who was presumably already far from starving. The heavier meal —1,051 calories and 10 oz. (300 g.) of steak—was certainly substantial but would not lie heavily on the stomach of an active man two and a half hours after ingestion. It would be more interesting to have the results of experiments in

[1] *J. Nutrit.*, 1946, **31**, 525.

which the performances of normal subjects were compared with those of men suffering from either real hunger or a gross surfeit. But possibly if the volunteers had been asked to swim after starving for a day, or thirty minutes after 2,000 calories in the form of roast pork and plum pudding, they would not have shown the willing co-operation which was necessary for the success of the experiments.

ANTENATAL PAEDIATRICS

At a famous children's hospital governed by a charter which limits the upper age for patients to 12 years the medical staff recently asked the board of management for permission to treat pregnant women, on the grounds that they sought thereby to influence the unborn child. This would have pleased Ballantyne, sometimes called the father of antenatal care. In his early work he wrote of attempts "to cure before birth the disorders and diseases of the foetus." This quotation was recalled by L. G. Parsons in the fifth Blackader Lecture, delivered in Canada last year and now available in printed form.[1] Recent events and discoveries have added particular interest to the problem.

"There is considerable evidence that as a result of rationing and better distribution of food the diet of a large part of the population has improved during the war years," and after a careful analysis of all the factors concerned Parsons concludes that the stillbirth rate and the neonatal death rate have fallen in part as a result of the improved nutrition of the mothers. The diet in the last third of pregnancy is of special importance. The mother transfers not only nutrients to the foetus but also certain immune bodies. The whole question of transferred immunity is ripe for reconsideration in the light of the estimation of serum proteins in the newborn and especially of the gamma globulin protein. Original work on this point must be interpreted with caution, because of the variations in placental structure. On the negative side, so to speak, Parsons mentioned the effects of diabetes in the mother upon the foetus and newborn baby, and the alarming and fascinating story of rubella and foetal deformities. Careful treatment of diabetic mothers will further reduce the risk of stillbirth, neonatal death, or gigantism. Australian investigators have suggested that pooled or adult serum should be given to the pregnant woman to confer immunity to the risks of rubella, but according to Parsons stocks are not available in this country.

In recounting the story of the rhesus factor the lecturer modestly refrains from explaining how right the Birmingham school were to insist that haemolysis is the primary lesion and the erythroblastosis the result of blood destruction. It is sometimes argued that undue prominence has been given to the rhesus factor, but Parsons quotes Haldane to the effect that congenital haemolytic disease is responsible for more deaths than any other inherited disease, possibly for more than all of them put together. For this reason it is wise to test the serum of every expectant mother against the Rh factor—in her own interest as well as that of the baby. Routine Wassermann testing has already been widely accepted. Both tests have the support of obstetricians, among them Prof. F. J. Browne, who has long and wisely taught the exact value of antenatal care. The eighth edition of his little book, *Advice to the Expectant Mother*,[2] has just appeared and celebrates its twenty-first birthday with a new short section on relaxation in pregnancy and labour. Here is antenatal paediatrics translated for the benefit of the mother. The close co-operation now being achieved between obstetricians and paediatricians is a good augury for the future of the young infant.

[1] *Canad. med. Ass. J.*, 1946, **55**, 327.
[2] Edinburgh: E. & S. Livingstone Ltd., 1947. P. 50. Price 9d.

THE KENNY METHOD

With the present widespread incidence of poliomyelitis attention is once more drawn to the method of treatment advocated by Miss Kenny—a method which incidentally has led her to formulate new and unusual theories of causation. Before the war the London County Council gave Miss Kenny facilities for a twelve-months trial of her method at the Queen Mary Hospital, Carshalton, and a report of this was published at the time in this *Journal*.[1] We commented then that Sister Kenny's work had drawn attention to the fact that in some instances treatment by splinting and other methods of fixation had tended to become too stereotyped. We also observed that Miss Kenny and her then co-worker, Dr. F. H. Mills,[2] were unduly optimistic about the results to be expected from the Kenny method. Miss Kenny, for example, then claimed that all cases treated by her from an early stage recovered completely—a claim not substantiated by the account of the cases given in the L.C.C. report. In short, Miss Kenny performed a valuable service in showing the benefits of devoted nursing carried out with an intensity and attention to detail unfortunately not possible in the presence of a large epidemic and a shortage of nurses. Miss Kenny went to the U.S.A. and succeeded there in obtaining some medical support for her "new concept" of the disease.[3] Miss Kenny's mind concentrated on the painful spasm of muscles in poliomyelitis, and she advocated early and active treatment combined with the local application of heat to overcome this spasm. On this one clinical fact of muscle spasm Miss Kenny built a theory of pathology which has failed to convince the leading authorities on poliomyelitis in this country and in the U.S.A. The spasm became the "primary lesion." Secondary to this was what was described as "mental alienation," showing itself in flaccid paralysis of muscles antagonistic to those in spasm. A valuable report on the results of the Kenny treatment in the U.S.A. was drawn up by an expert committee and published in 1944.[4] In this it was pointed out that treatment by hot wet packs and hot baths had been advocated by medical men in 1917, 1922, and 1936; so, clearly, Miss Kenny had discovered nothing new in treatment, though she may have performed a useful service in reminding the medical profession once more that such method of treatment was valuable. The committee criticized many of Miss Kenny's statements and concluded that (1) "There is no evidence that the Kenny treatment prevents or decreases the amount of paralysis . . ."; (2) "In several cases seen by us the paralysis progressed after the Kenny treatment was instituted"; (3) "While the committee disapproves of, and condemns, the wide publicity which has misled the public and many members of the medical profession, it acknowledges that this has stimulated the medical profession to re-evaluate known methods of treatment of this disease and to treat it more effectively."

Dr. Elliott C. Cutler, Surgeon in Chief of the Peter Bent Brigham Hospital, Boston, Mass., has been elected President of the American Surgical Association, and the Boston Surgical Society has awarded him the Honorary Jacob Bigelow Gold Medal. The U.S.A. War Department has also honoured Dr. Cutler by conferring on him a second Distinguished Service Medal.

[1] *British Medical Journal*, 1938, **2**, 852.
[2] Ibid., 1937, **2**, 414; 1938, **1**, 168
[3] *The Kenny Concept of Infantile Paralysis and its Treatment*. 1943. St. Paul, Minneapolis, U.S.A.: Bruce Publishing Company. See also *British Medical Journal*, 1943, **2**, 141, and 1944, **1**, 627.
[4] *J. Amer. med. Ass.*, 1944, **125**, 466.

RECENT CANADIAN RESEARCH ON INSULIN

PROF. CHARLES BEST'S BANTING MEMORIAL LECTURE

The first Banting Memorial Lecture, under the auspices of the Diabetic Association, was given at King's College Hospital Medical School on July 18 by Banting's collaborator, Prof. Charles Best, F.R.S., professor of physiology in Toronto. The company present, who packed the lecture theatre to capacity, included Lady Banting, now Dr. Henrietta Banting, who has recently completed her internship in Toronto, and is doing post-graduate work in London.

Dr. R. D. Lawrence, who presided, mentioned that last year the twenty-fifth anniversary of the discovery of insulin by Banting and Best was celebrated all over the world. The Diabetic Association in London was founded in 1931 and now had a membership of 11,000. When the tragic death of Sir Frederick Banting took place in 1941 it was proposed to establish a convalescent home in his memory, but war and post-war conditions made such a project impossible for the time being, and meanwhile the Banting memorial lectureship had been instituted.

Study of Carbohydrate Metabolism

Prof. Best said that he would not attempt again to pay tribute to Banting nor to say what Banting had meant to him and to medical research generally. The study of insulin and carbohydrate metabolism had recently been intensified by certain practical considerations, among others the realization that the use of insulin was constantly increasing. He suggested that it was the responsibility of health departments of Governments to enforce general collection of pancreatic glands, to decide whether the pancreas should be used for insulin production, for amino-acid digests, or for the tanning of leather, to investigate sources of insulin hitherto not considered feasible, and to promote the study of insulin chemistry. It was not his intention to discuss these practical considerations further, nor could he in three-quarters of an hour give a well-rounded account of recent advances in all aspects of carbohydrate metabolism. It had been suggested to him that he should take the various work proceeding in his own laboratory at Toronto as an illustration of current trends, and he would therefore discuss briefly the main lines of research which he and his colleagues were pursuing.

It would perhaps be remembered that before the war R. E. Haist and he carried out some work on the various influences which might affect the insulin content of the pancreas, as, for example, the profound decrease in insulin content produced by fasting. It was shown that the administration of insulin lowered the insulin content of the pancreas. Further clinical research along this line had been almost completely inhibited by one obstacle, namely, the inability to give insulin to the non-diabetic child of diabetic parents without the danger of producing psychological trauma. He was not talking about routine treatment but clinical research. A great advance would be made if such clinical study could be made possible. Some clinicians might perhaps take up the subject with a sufficient number of controls to determine whether there was any application of the experimental work in the clinical field. He did not think there was any contraindication to such studies beyond the great trouble involved and the risk of psychological trauma in the non-diabetic subject. The study would have been carried out long ago had it been possible to give insulin by the mouth.

Islet Cell Investigation

Dr. R. E. Haist and his group had now developed a new technique for total islet cell investigations. Under the ordinary microscope the results might appear to be without flaw, but when the phase microscope was used it was revealed that in some cases corrections had to be made. A special technique had now been worked out for the exploration not only of the known variables affecting insulin which were studied years ago, but many new ones. The increase in islet volume with age in growing animals had been noted, but the islet volume per weight had been found to decrease with age. Much work had still to be done on the islet volume of the pancreas.

Dr. Collins-Williams and Dr. Wrenshal had evolved a useful method for estimating insulin in amounts too small to be assayed by ordinary procedures. Actually it required much less insulin to lower the blood sugar of a mouse than it did to produce convulsions. Amounts of two-hundredths of a unit of insulin could be assayed very accurately. This enabled a determination to be made of the amount of insulin in the pancreas of a small rat, representing perhaps 100 mg. of tissue.

It was decided to study very accurately the total insulin content of each pancreas of diabetic rats. In many animals the matter became complicated by the fact that, when they became diabetic with the high blood sugar, not all remained diabetic after alloxan, and the return to a non-diabetic state was not uniform; some animals got better quickly, others gradually, so that the study was much more difficult than had been expected. It was not possible to rely on the animals being constantly diabetic although initially hyperglycaemic, and each animal had to be evaluated individually. Williams and Wrenshal on his staff were studying the return of the insulin content of the pancreas in diabetic rats under various conditions. It was hoped that this new microtechnique for insulin assay would make it easier to determine the activity of beta cells in islet tumours. Some tumours had very active beta cells which grew well *in vitro*, but others were disappointing. In some work done in Montreal by Sergera it had been possible to produce remnants of pancreas containing islets with almost exclusively alpha cells present and others with almost exclusively beta cells. By ligation of the pancreatic ducts in the tail of the pancreas in small dogs a preparation was obtained made up almost entirely of alpha cells, while in the body of the pancreas a preparation was forthcoming consisting almost entirely of beta cells. Competent histologists in this line had verified these results. A preparation could be obtained which was predominantly of either alpha or beta cells, and his colleagues were now engaged in assaying with the new technique the pancreatic remnants for insulin. No results had so far been obtained. Prof. Best suggested humorously that it would be in accordance with transatlantic tradition if at that moment a cable were handed to him announcing important results. It would certainly be amazing if the preparation containing almost entirely alpha cells turned out to have the higher insulin content. He was prepared for such a happening, though he had not seen any good evidence as yet that alpha cells performed any separate function.

Transplantation of Tissue Culture

It was well known that there had been numerous attempts to transplant tissue cultures of islet cells, but these had been unsuccessful. Although, on looking through the literature, nothing of this appeared to be recorded, on asking various workers it was evident that many unreported attempts had been made. In Leyden, Holland, which he had recently visited, an interesting experiment in tissue culture was recounted to him by Prof. Gaillard. Active islet cell tumours were taken and cultured in tissues with gradually increasing concentration of the serum of the potential recipent. A good deal of work had been done in Leyden in this manner, and two successful cases were recorded in diabetic patients who had previously been taking 80 or 90 units of insulin a day and had been able to get along without insulin now for two years. Separate research, however, was needed in respect of each case. It was not possible by routine procedures to obtain a good growth of islet cell tumour.

The microtechnique of insulin assay was being used by Wrenshal and Williams to determine the insulin content of the pancreas of human diabetics, which was in some instances too small to be assayed by ordinary procedures. Too much emphasis had been laid on the fact that the pancreas of the diabetic did contain insulin: it would be better to emphasize that it contained far less insulin than the normal. It was difficult to get the material under standard conditions, but it was hoped that the data which were being accumulated might eventually show the range of insulin content of the pancreas of well-established diabetics.

A reliable procedure for determining the very small amounts of insulin which were thought to be present in blood would be of great value. There were indirect procedures for making such estimations. One method had been to give a constant

intravenous injection of insulin to depancreatized dogs. The same individual animal on repeated tests gave very constant results, though there was considerable variation between different animals. Work on the completely depancreatized patient needed very careful scrutiny because the digestion had been altered; the digestion of food was not the same after removal of the pancreas. What one would like to see was a comparison between the normal person and the depancreatized patient who nevertheless was absorbing the same amount as the normal, was of the same weight, and so forth.

It was well known that other glands interfered greatly with the action of insulin, and if some of these glands were taken out the animal was much more sensitive to the substance. After removal of the adrenals the sensitivity was increased by about five times. It would be an interesting piece of research to take out the pituitary and both adrenals and at the same time make the animal diabetic, but that was a great test of technique. He thought they were nearly at the point at which they could pick up the insulin content of the blood. In these and other investigations much more could be done if finer methods of estimation were available, and it would be possible then to use the terms hyper- and hypo-insulinaemia with considerable confidence.

Effect on Enzymes

Prof. Best went on to say that it was not his intention to deal with the present state of knowledge of the multiple effects of insulin. A good case could be made for a fall in blood phosphates, in blood potassium, and in ketone bodies in the blood. Work had been done on hexokinase by the Coris showing that the inhibition exerted by the pituitary and the adrenals was always relieved by the addition of insulin. Another enzyme system recently shown by Cori to be affected by insulin was phosphorylase. It was interesting that the factor which caused the initial hyperglycaemia caused breakdown of liver glycogen. The hypoglycaemic factor of insulin could be completely destroyed by mild alkalis, but the part that remained after the anti-diabetic factor of insulin was destroyed caused a rapid short-lived hyperglycaemia in certain animals and also a breakdown of glycogen, that is, the reverse of the effect of active insulin.

He had little to say on the use of isotopes in carbohydrate metabolism. They had been limited by the scarcity of isotopes, but they had plenty of radio-active phosphorus. With the help of a new mass spectrograph in his department they were hoping to study certain problems of carbohydrate breakdown.

Finally he turned to a more general subject and gave a brief review of the work of De Witt Stetten and his colleagues. It illustrated better than most other findings the importance of labelled molecules in the study of carbohydrate metabolism. Under normal conditions there was a fairly constant composition of tissue, but this was not due to the lethargy of the molecules in the tissue, it was due to the fact that there was a steady interplay, an active interchange in and out. By using certain procedures Stetten and his colleagues calculated the amount of glycogen synthesized each day under certain conditions in rats. The amount was about 0.44 g. each day, the rat eating about 15 g. of carbohydrates, or about thirty times as much as would be required for the synthesis of this quantity of glycogen. Ten times as much of the glucose eaten was turned into fat as was turned into glycogen. The suggestion was made that lipogenesis was inhibited in the diabetic, as a result of which an appreciable amount of glucosuria might be expected unless the defect were compensated by other mechanism. The total fat synthesized in the diabetic rat was only about one-twentieth of that in the normal animal. The amount of glucose which appeared in the urine of the rat corresponded fairly closely with the amount the animal failed to utilize for fat synthesis. In this way it was possible to study the urinary glucose of the animal and to fractionate it and determine at any one time how much of the glucose came from the carbohydrate of the diet and how much from gluconeogenesis.

All these new studies supported the view that glucose was not formed from fatty acids under any conditions with which we were familiar. Some of the conclusions at which Stetten had arrived and which had been confirmed by others bore out the older findings and at the same time opened up a number of new problems. It was obvious that clinicians and physiologists must work very hard to keep abreast of the rapid advances of knowledge of carbohydrate metabolism which the modern techniques were making possible.

FUTURE HOSPITAL ADMINISTRATION

SIR ARTHUR RUCKER'S ADDRESS

The Institute of Hospital Administrators held its annual conference at Brighton on April 19, the Chairman of the Council, Mr. B. Lees Read, presiding over the earlier part of the proceedings, and the president, Mr. Charles G. Rolliston, over the later.

Sir Arthur Rucker, addressing the meeting on "Hospital Administration in the New Health Service," said that the last idea the Ministry of Health had was that they were going to administer the hospitals. "We want you to tell us how the hospitals have got to be administered. There are others who must join with you in telling us, but the professions concerned must tell us how the hospitals must be administered. Our job is to build up the background of administration by which you can do your job." The chief difficulty they had had to resolve in the framing of that part of the Act was how to "marry" two somewhat contradictory ideas. They wished to make sure that the professional people who had to make the scheme work would have the fullest opportunity of taking their part in the framing of the policy of the Service, and in running and administering it. Against that they had to be careful not to frame a service that would be pure syndicalism. In this country they did not look with favour upon the idea that the people who were employed in a particular service should also be its managers.

In the Schedule that dealt with the Central Health Services Council there was a provision for the inclusion in the Council of five representatives of hospital management. It was fairly obvious that the experience of the Institute would have to be included in that representation. In addition to that it might or might not prove desirable to have a standing advisory committee on hospital services.

In trying to frame these services there was another problem that had had to be resolved. That was the old problem of "centralization or decentralization." In the new health service insurance contributions and, to a far larger extent, the taxpayers' money would have to be brought in. That being so, the old saying about the "piper" and the "tune" must operate to some extent. The duty of providing the money for these services could not be put on to the Exchequer without placing the responsibility for the services upon someone directly answerable to Parliament. That was why, ultimately, the Minister must be responsible for these services, because he, and he alone, could be answerable to Parliament. That did not mean that the actual operation, administration, and management of the services needed necessarily to be concentrated in Whitehall. They had sought to do it in the hospital service by setting up Regional Boards, with management committees under them to whom the maximum degree of responsibility would be directed.

There was one point of real difficulty which ought to be stressed. That was the relationship between the local authority services and the hospital services. Under the Act all institutional provision for maternity would be the responsibility of the hospital services. The provision of a midwife and medical care for a woman being confined in her own home would be the responsibility of the local authority. That might well lead to difficulties. Suppose a woman proposed to be confined in her own home and made arrangements with the local authority for a midwife to attend her, and then, towards the end of her pregnancy, or worse still after parturition had started, something went wrong and she required admittance to a maternity hospital. She then had to pass from the care of the local authority to the care of another authority. That was untidy, but it had been put into the Act because the only alternative had been to take over the entire local authority services, and that, the Government thought, would have been neither practicable nor desirable.

Under the Act all the local authority services were to be the responsibility of the counties and county boroughs. Functions relating to child welfare were delegated to the divisional executives and the excepted areas which were set up under the Education Act. That had been done because it had been thought that child welfare should accompany the care of children in the educational field, but an interesting point had arisen. Lancashire, for example, were working out a scheme at the moment which was not dissimilar to the arrangements for London, under which the county council would like to set up committees throughout the county area for the administration of all the local authority health services, keeping them all together. They would then co-opt representatives of the minor authorities on to these committees. That differed a little from the scheme contemplated in the Act in that it covered all the local authority services, not only child welfare. The administration would be by committees of the county council, as to which members of the local authorities would be co-opted, instead of by delegation to divisional executives and the excepted areas under the Education Act. It would mean bringing all the health services under local authorities in the counties into administrative areas which would correspond broadly with the groupings of hospitals in the hospital service, and there might be some advantage in that.

Hospital Services

Already they had made a start. The areas of the Regional Boards had been defined and had been approved by Parliament. They hoped to constitute the Regional Boards in a very short time, and nearly all the chairmen who had been invited had already accepted their appointments. The Minister was considering the recommendations for the appointments of members of the Boards, and it was hoped that the Boards would be in being shortly. The Minister must retain the ultimate financial control; nevertheless, he would delegate to the Regional Boards the responsibility for the planning of the hospital services in their area. Just as it was no part of the Minister's function to try to manage hospitals, so also it was no part of the job of the Regional Boards to manage the hospitals. Their job was to arrange the pattern of the hospital services in their region, and to survey their area and see whether the services were adequate.

The first job of the Regional Boards would be to group their hospitals into a sensible pattern and to appoint management committees for each group. Most hospitals, perhaps every hospital, would require a local house committee to look after the details of organization. That was the chain: the Minister, the Boards, the management committees, and the house committees. The new feature of importance was this grouping of hospitals under the management committees. In the past, hospitals in many areas had been too much isolated units, and had been almost in competition with other hospitals in the area.

As always, there was the other danger that if the management group was too big the local interest might be lost. They wanted to keep local patriotism—the feeling that it was "their own hospital"—but was there any reason why they should not get the feeling that it was their own *group* of hospitals?

In some ways the Regional Board would be a body not unlike the local authority, except of course that it was not elected by the local electors. It would be a body of experts and common-sense people whose job would be to give general decisions on policy and so on. They would need a competent, and he feared a substantial, staff. At that level the planning of the services was largely a medical affair, and they looked to the chief medical officer of the Regional Board for that. They did not want to have a doctor over a layman, or vice versa; they must work together; but they did think the doctor's the most important post. When they came to the management committee, which would deal with the day-to-day management of the hospitals, seeing that the hospitals were economically run and providing all the services needed, they must not be too dogmatic. It was primarily a layman's job, but doctor and layman must work together. The areas were not rigid in any sense. It was not the intention that anyone who fell sick in one Region should be required to go into a hospital in that Region. Still less should each management committee have a rigid area for which it was responsible. Any patient would be free to go to any hospital anywhere.

The success with which they achieved that idea of an ultimate control at the centre with a genuine decentralization of administration would depend largely upon finance. An annual budget would be fixed for each Regional Board. Within that budget the Regional Board would be free to manage its own affairs, subject only to the approval of any unusual expenditure which was outside the budget. Similarly, each Regional Board would approve the budget of the management committees within its region. But, the scale of expenditure having been determined, the management committees and the Regional Boards would then run their own affairs at their respective levels. There were other provisions by which they were to have their own money: the carry-over of endowments. In the case of the teaching hospitals that money would be their present endowments. In the case of the management committees it would be their share of a general pooling of all present endowments.

Central Purchase of Supplies

Considering the question of supply, he said that their conception at the Ministry was that in due course it might be necessary to purchase centrally on a fairly substantial scale. Here again there was this question of balance. The last thing they wanted was a too rigid standardization of supplies, and they must carefully balance the advantages that could be obtained from sensible central purchase with the dangers of over-standardization. They would have to set up a central supply department at the Ministry, but at the outset of the new Service the existing supply arrangements should, so far as is possible, run on. In the meantime all they would do centrally was to look at the fields of shortages, and, where shortages existed, place central orders. Some were now being placed.

The teaching hospitals would remain outside the purview of the Regional Boards, and be managed by their own boards of governors, who would be responsible for providing the hospital facilities required by the medical schools for undergraduate teaching. A hospital taking part in postgraduate teaching would not necessarily be regarded as a teaching hospital. So far as the Board of Control was concerned with the administration of mental hospitals, that administration would go over to the Ministry of Health. The Board would, however, remain in being as the body responsible for questions relating to the liberty of the subject. That step would be taken quite soon, and circulars would be sent out suggesting the steps to be taken to bring the mental hospitals into the whole picture. It would often be impossible to bring the mental hospitals into the same management committees as the other hospitals. The mere size of mental hospitals was often such that it would not be possible, but the link between the general hospital and the mental hospital would be widely developed and encouraged, even when an actual merging in a single management committee was impracticable.

The Regional Boards would take the very big responsibility of ensuring the proper distribution of specialists. A vacancy in a hospital would be advertised, and there would be applications from various consultants to take that post. The local management committee would then sit with the Regional Board to appoint a selection committee to recommend suitable candidates.

What was the hospital problem to-day? In this country there were about 130,000 beds in general hospitals, 11,000 maternity beds, about 40,000 beds in isolation hospitals, and about 60,000 for chronic cases. In the mental hospitals there were something like 127,000 beds, and altogether they had a grand total of about 400,000 beds. They had not very accurate figures, but nearly 40,000 beds in general hospitals were closed, mainly due to lack of staff. They had rather more accurate figures of the mental hospitals, where there were some 16,000 beds which could be in use but were not. Of these, 11,000 were at present being used for other purposes; about 2,000, which had been diverted during the war, they were trying to get restored, and about 3,000 were closed because they could not be staffed.

They were not going to have a proper hospital service until they could solve the staffing and building problems. The

nursing part of the staffing problem was the most acute, and there were signs that the domestic staffing problem, which had been very acute, was improving. There was not much improvement in the nursing problem. They had had a working party sitting on that problem, and it had produced an exceedingly interesting, perhaps provocative, report. It would be published soon. They had promised not to give effect to that report until they had obtained the views of all who knew the subject, but, that being done, they would get something of value for the long-term solution. He was not sure it would help much in the short-term. Emphasis was likely to be placed on the importance of making sure that student nurses really were students, thereby helping to overcome what was a main cause of shortage—the wastage of nurses. They were getting enough young women, and men too, coming into the profession, or nearly enough, but the trouble was that they did not stay. They were also setting up a similar working party on the allied problem of midwifery.

Building was a very big problem. The Ministry had tried to get all they could for the hospitals against the competition of housing, factories, and all the other sorts of building, and they had not been doing too badly. They had had priorities amounting to about £4,000,000 a year for hospital affairs, but, of course, the amount that ought to be spent on hospitals in this country was astronomical.

Sir Arthur Rucker concluded by referring to the deep interest overseas in what they were doing. They had the most magnificent opportunity that had ever been given to public health administrators. Let them trust each other and work together for a good service.

Replies to Questions

A discussion then followed, and in reply Sir Arthur Rucker said that the boundary-line difficulties had been magnified in the past because there had often been two authorities who were watching that boundary line very jealously. There could not be the same jealousy between a national service and a local service. Answering another question on who sacked the staff, he said that technically the hospital staffs would be the employees of the Regional Board, but, with the exception of the specialist staffs, the Regional Board would delegate the appointments and dismissals to the management committees. In any service of this kind there could only be satisfactory administration if there was joint administration by administrator and by doctor. Of course matrons and all the other services must have their part.

He had been asked about the working-men governors. At the moment there were all sorts of bodies taking an interest in hospitals—societies with contributory schemes, and so on. But clearly that could not go on in the same way; it would not be reasonable to expect the people to contribute when they had to pay a national contribution. There might well be a great deal in the principle, though in different ways, of having local friends of the hospitals. There would be opportunities for them to bring to the hospitals the voluntary services which would be needed still.

He was not convinced that one should think of hospital administrators as a completely separate class of the community, to be trained or selected for that purpose and that service only. Administration was not a science, it was an art. With regard to the point about mental hospitals it was important to "marry" the mental service with the general hospital service. The development of mental wards and the interchange of consultants was something they wished to see in future.

Of postgraduate teaching he said that they had not contemplated that a hospital would be dealt with as a teaching hospital, and would be outside the purview of the Regional Board and have its own board of governors, merely on the grounds that it was a postgraduate teaching hospital. There were many opportunities for a teaching hospital and its medical school to be associated with other hospitals—for instance, in the Norfolk and Norwich Hospital there was a link with Cambridge University, and a number of the consultants at the Norfolk and Norwich were on the staff of the medical school at Cambridge. Such links would be welcomed.

Referring to the difficulty of dealing with old people who occupied accommodation in mental hospitals but who did not really require treatment, he said that the scheme would not really be complete until they reached the final stage of it—the rewriting of the Poor Law. That would be done in a Bill to be introduced in the next session of Parliament. In the case of convalescent homes every one had to be looked at in detail. They were only entitled to take over hospitals as defined in the Act, so that where a convalescent home was within the definition it would come under the scheme.

The health centres were not going to be hospitals but common surgeries at which general practice would be conducted, with some diagnostic facilities, but they did not yet know about the precise arrangements. The link between the health centre and the hospital would be much the same as the link to-day between the practitioner and the hospital. He did not think there was anything in the scheme which would prevent a medical man moving from Region to Region. Probably there would be a tendency for consultants to serve hospitals in one Region, though they might move to another post elsewhere. The management committees would be concerned to see that they did not get some doctor "wished" upon them whom they did not want.

THE MIDWIFERY WORKING PARTY

Last April a Midwifery Working Party was set up by the Minister of Health and the Secretary of State for Scotland to inquire into the recruitment and training of midwives and especially to consider the reasons for and the manner of overcoming the present shortage. The Working Party, desiring to obtain a complete picture of the conditions in the profession, has drawn up a questionary which is being sent on Aug. 8 to all midwives throughout the country who in 1944 notified their intention to practise and also those who qualified in 1946. These years have been selected in order to give a random sample. The questionary is designed to find out if and why a woman gave up midwifery after training, the type of work she has been doing in midwifery, whether her practice is urban, rural, or mixed, what additional qualifications she may possess, and whether she needs a midwifery qualification for her present post. It ends with the leading question: "On the whole do you feel satisfied with midwifery? If not, why are you dissatisfied?" A letter which accompanies the form explains that the information is wanted for statistical purposes only, that the replies will be treated as confidential, and that the members of the Working Party will not themselves see the actual forms but only the tabulated statistics.

To find out the cause of the wastage of midwives after training is one of the principal objects of the inquiry, and therefore it is hoped that non-practising as well as practising midwives will return the forms. A pilot questionary which has already been circulated elicited 60% of replies, but the percentage of replies to the nation-wide circular must be higher than this if it is to be of real value. The statistical analysis will be undertaken by the Social Survey Office. A separate inquiry is being made of training schools to find out how many candidates take Part I only of the C.M.B. examination and the reasons for not proceeding to Part II. The Working Party, which appeals for any further evidence or suggestions, expects to present its report early next year—probably in March.

Since last autumn 26 shortened courses have been in operation to enable ex-Service men and women qualified as 1st class nursing orderlies to become State registered nurses in one year instead of by means of the usual three years' training. There will be vacancies for these courses next October, and applications from those suitably qualified should be made at once to the Secretary of the Ministry of Health, Whitehall, London, S.W.1. Only those with the rank of nursing orderly or nursing member class I, leading sick berth attendant, and L.A.C.W. or L.A.C. in the trade of nursing orderly who have had at least two years' ward experience under trained nurses are eligible. Men and women still in the Forces should apply through Service channels. Men are paid at the rate of 92s. a week with a deduction of 30s. for board and lodging, or 20s. in the case of married men with home responsibilities. Women receive £90 a year and free board and lodging or a living allowance of £80 if living at home. Examination fees are paid and free medical treatment is provided. Students may be accommodated at the training centre or live at home.

Correspondence

Limits of Certification

SIR,—I was asked by the Civil Service Commissioners to examine from the psychiatric standpoint candidates for the Civil Service "in which there is some doubt or in which candidates appeal against the findings of the medical examiner." They asked for a full and detailed report and stated in a letter that they felt that an opinion of this kind would place them in a better position to decide on each candidate. I objected and said that I would be willing to certify only that there was no medical reason why a man should not be accepted, or that there was some medical reason why he should not be accepted. The Commissioners then wrote a long letter outlining exactly what they did and why they wanted such a full opinion on each candidate referred to me. I asked for their permission to show this letter to my colleagues. I received a very dusty answer: "You will kindly regard as strictly confidential to yourself the information concerning their practice conveyed to you in their letter of Feb. 19. . . ." "As the Commissioners apprehend that you still feel reluctant to oblige them. . . ." Since then I have not been asked to see any case for them, and presumably somebody else is doing so.

To my mind this raises an important point of principle. Surely as medical men we are not expected to select candidates or to say that candidates would be suitable for the Civil Service. We can say in certain cases that for medical, psychological, or psychiatric reasons a man would not be suitable, but I do not see that we should be called upon to do more than this. Briefly the medical role, as I see it, is not to choose the First XV but to pass men simply as fit or unfit to play. In making this limited decision, which I think does fall within the medical province, it would be much easier to form an opinion if the candidate knew that anything he said confidentially would not be passed on to the Civil Service Commissioners, although of course he would know that an opinion in general terms would be given as to whether he was or was not fit for the Service; for in these circumstances candidates would surely speak more freely. This would not be the case if candidates knew that a detailed report of what they said was to be put away in a Government file and perhaps seen by numbers of laymen.

It seems that there is no medical man on the Civil Service Commission. Reports of this kind, perhaps dealing with complicated technical points, would therefore be considered by a lay body and might well be misinterpreted. I doubt if anybody would object to sending a full report confidentially to a suitable Ministry medical officer, who would then have the duty of interpreting it to the appropriate lay body. I dislike, however, the whole idea of passing on confidential and perhaps intimate information obtained in a professional capacity to lay people.

At the moment this apparently minor problem concerns only candidates for the Civil Service. With the steady extension of Government control in industry and in our own profession the principle is one which may well concern many more people in the near future than it does at present. What is needed, it seems to me, is an authoritative ruling on the limits of certification intended for the use of lay bodies.—I am, etc.,

London, W.1. DESMOND CURRAN.

Reporting of Deaths to Coroners

SIR,—Many practitioners are seriously disturbed by public comment, recently expressed by the coroner who conducted the inquest in the Clements case, on the subject of the conduct of post-mortem examinations of persons who have died from unknown causes. Since such doubts are prone to cause confusion and irregularity of action among practitioners generally it is thought desirable to recite afresh in an abbreviated form an authoritative opinion obtained from Mr. (now Sir) Roland Burrows, K.C., dealing with the questions that are raised. He maintained in his opinion:

(1) That there is no legally enforceable duty resting on a medical practitioner *qua* medical practitioner to report any death to a coroner.

(2) That a coroner is not vested with any power to require a practitioner to report any death.

(3) That the registrar of deaths is vested with a duty to report deaths in certain circumstances to the coroner.

(4) That a practitioner must not do anything to obstruct a coroner in the discharge of his office.

(5) That a practitioner may make a post-mortem examination of a person deceased with the consent of the deceased's relatives whether or not he knows the cause of death, unless, by so doing, he knowingly hinders the coroner in carrying out his duties; but, as soon as it comes to the knowledge of a practitioner that a coroner has been informed from any source touching the death of the person involved, an examination of the body by that practitioner should not be made in these circumstances without an instruction from the coroner concerned.

These are the legal duties of medical practitioners, but, of course, like other members of the community they have social, public, and moral obligations to discharge which are not enforceable by law, and such duties may include one to assist a coroner in certain special circumstances. It is desirable that practitioners and coroners should collaborate harmoniously for the public good, and it is hoped that every practitioner whether engaged in hospital or private practice will refer to the coroner any death respecting which he entertains any doubt as to his responsibility or obligation.

It may perhaps be not inappropriate to remind your readers that at the moment a Committee of the British Medical Association is examining and will report upon the operation of the Coroners Acts where they impinge upon the work of medical practitioners. This committee contains among its personnel several distinguished coroners whose opinions in discussion are greatly valued. It is hoped to furnish a report towards the end of the year for consideration eventually by the Representative Body of the British Medical Association, and it is believed that this report will cover adequately many of the problems that arise in the course of medical practice affecting jointly medical practitioners and coroners in the discharge of their legal and professional duties.—I am, etc.,

ROBERT FORBES,
London, W.C.1. Secretary, Medical Defence Union.

The Thalamic Dysfunction Syndrome

SIR,—The dys-symbolic effusion of Dr. B. H. Kirman (July 19, p. 109), criticizing my article on the use of euphoriants in depressive states, is a masterpiece of prejudice, mis-statement, and inaccuracy. In the first place the term "thalamic syndrome" used by Dr. Kirman is a gross terminological error, the term used to denote the condition in my paper being "thalamic dysfunction syndrome." The former expression is already in general use by neurologists to describe an entirely different disorder, namely, a unilateral gross lesion of the cortico-thalamic fibres accompanied by a definite sensorimotor syndrome. In this connexion it may be pointed out that, contrary to Dr. Kirman's assertion, motor symptoms are a recognized feature of lesions of the thalamic-basal ganglia complex.

With regard to the question of what constitutes a "higher centre," it is now well known that the thalamic centres and their cortical connexions are concerned in some of the most complex cerebral functions, particularly in the sphere of emotional expression and feeling tone. This is demonstrated by the personality and affective changes following prefrontal leucotomy, in which operation the principal tracts severed are the fronto-thalamic connexions, and by the characteristic mental changes found in post-encephalitis and other diseases of the basal ganglia. Dr. Kirman attributes to me two statements which were certainly not made in my article. These are that tremors, obsessional thoughts, pseudo-hallucinosis, etc., are thalamic and not cortical in origin, and that the various psychic functions can be strictly localized to individual parts of the central nervous system.

Dr. Kirman refers in his letter to "the clumsy attempt to divide off 'neurotic depression' artificially from psychotic depression." My experience with a large series of treated cases has shown that the two conditions can, in fact, be so differentiated by the specific response to anoxic therapy, which differs radically in the two types of affective disorder. Again,

he states that I have attempted "to divorce it (the thalamic dysfunction syndrome) . . . from environmental factors"; whereas in my paper I stated clearly that "the thalamic dysfunction state may be regarded as a response of the organism to stresses of various kinds" (i.e., environmental stress, conflicts, toxins, and so on).

With regard to his remarks about the morphine and cocaine addiction syndromes, if Dr. Kirman were to go to the trouble of consulting any of the standard psychiatric textbooks dealing with the subject, he would find it stated that alkaloid addiction differs in a number of important respects from alcoholism. This last-named toxin, incidentally, is a cortical depressant rather than a true euphoriant of the type described in my article, in addition to being chemically and pharmacologically unrelated to the agents under consideration. Finally, while admitting "the limited value of present methods" (i.e., of psychiatric treatment), he is apparently unable to suggest any alternative or more effective form of treatment than that suggested in my article. In other words, his criticism is the purely destructive kind which questions everything but decides nothing, containing not one single constructive contribution to the problem under discussion. I should, of course, welcome any constructive suggestions or comments on the new concept of affective disorders put forward in my paper and the pharmacotherapy of these conditions. But it is a pity that Dr. Kirman did not take the trouble to read the paper through properly before erupting so impulsively into print.—I am, etc.,

London, S.E.6. G. TAYLEUR STOCKINGS.

Bornholm Disease in the Tropics

SIR,—Only a few weeks before the outbreak of Bornholm disease at Aden described by Drs. W. M. Jamieson and D. M. Prinsley (July 12, p. 47) there was an outbreak of an unusual nature in a Naval barracks at Singapore (June, 1946). The distinctive features were as follows: (1) It was larger than any recorded to my knowledge (over 100 cases). (2) It was explosive—more than seventy of the cases occurring in the first twenty-four hours. (3) It was sharply limited to European ratings in the Naval establishment concerned, the majority of cases occurring among men who fed at one end of a mess hall, but who worked and slept in different places over a wide area. (4) The primary lesion appeared to us to be in the parietal pleura, and in several cases a well-marked pleural rub ensued. Features 2 and 3 do not seem consistent with a contact infection, and contamination of food was suspected, possibly by flies. Otherwise signs, symptoms, course, and complications were as normally described.

There had been an outbreak of poliomyelitis at Singapore earlier in the year, during which a few civilians admitted to the fever hospital were regarded as probably suffering from Bornholm disease, but previously this does not appear to have been recognized in Malaya. A Dutch colleague, however, stated that he was familiar with the symptoms in sporadic cases in the Netherlands East Indies.

I was recalled to U.K. before our outbreak had entirely subsided, but a colleague remained to follow up the cases and we intended to produce a joint report for publication on his return. Unforeseen circumstances have so far prevented this partnership from delivering the goods.—I am, etc.,

Milsted, Kent. J. VINCENT SMITH.

The "Costoclavicular Syndrome"

SIR,—The greatest number of cases complaining of this condition are women, and the production of minor degrees of this condition may be by the shoulder strap of the brassiere. I have had three such cases in recent months, in which symptoms have been functionally relieved by doing away with the shoulder strap. The present passion for "uplift," no doubt encouraged by film stars, is not without its physical disadvantages.—I am, etc.,

Sunderland. W. GRANT WAUGH.

What is Folic Acid?

SIR,—In the article by Prof. L. S. P. Davidson and Dr. R. H. Girdwood entitled "Folic Acid as a Therapeutic Agent" (May 3, p. 587) it is stated that free folic acid is pteroylglutamic acid, and in its conjugated form is pteroylheptaglutamic acid. Your leading article (p. 604) stated, "Folic acid does not occur free in foods but as a conjugate with hexaglutamic acid, known as pteroylhexaglutamylglutamic acid. . . ." Wilkinson *et al.* in their article in the *Lancet*, 1946, quoting from Angier *et al.* (1946), hold that synthetic folic acid is a compound of 2-amino-4-hydroxy-6-methyl pteridine and *p*-aminobenzoylglutamic acid.

There seems, therefore, to be a difference of opinion as to what folic acid really is, both in its free and conjugated form.—I am, etc.,

Dublin. ALFRED R. PARSONS.

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Wilkinson, J. F., *et al.* (1946). *Lancet*, **2**, 156.

Hypertrichosis of the Lanugo Hair in Malnutrition

SIR,—With reference to Lieut.-Col. S. K. Roy's very interesting letter on achromotrichia in tropical malnutrition (March 22, p. 392), I should like to be permitted to call attention to a little-known condition also found in some cases of malnutrition, especially in children—viz., hypertrichosis of the lanugo hair.

This condition generally affects the lanugo hair of the legs, especially the extensor surfaces. The hair becomes much thicker, longer, and at times darker. It is often seen in times of war in children who, used to an abundant, well-balanced diet, have been placed suddenly, for reasons of necessity, on an insufficient diet particularly poor in animal proteins and fat. On giving the child again a proper diet the condition rapidly ameliorates and finally disappears.

It is interesting to note that the condition is well known to women of the working classes in the South of Europe. A woman who, for reasons of work or some other reason, has put her children in charge of neighbours or relations, will often complain on her return home that the children have not been well looked after and have been starved, "as shown by the thick hair on the children's shins."

The subject of lanugo hypertrichosis in general, as well as lanugo alopecias, is an interesting one, but is beyond the scope of this letter. I might mention, however, a peculiar form of lanugo hypertrichosis of the arms and legs which occurs in certain individuals every summer (summer lanugo hypertrichosis), in others (very few) every winter (winter lanugo hypertrichosis). The subject has been dealt with briefly in my little book *Diseases of Africa* recently published (Apollon and Co., Rome).—I am, etc.,

Lisbon. ALDO CASTELLANI.

Treatment of Hydrocele by Injection

SIR,—For many years several sclerosing substances have been used in the treatment of hydroceles with varying results. In a recent follow-up of patients suffering from hydroceles treated at this hospital in 1944, 1945, and 1946, 46 patients have been treated by injection of quinine urethane. Six patients have not been traced. Of the 40 patients traced all (with the exception of one still under treatment) have been successfully treated. Some of those treated have had hydroceles of long standing, some had previously been treated by repeated aspirations, and nearly all attended hospital seeking operative treatment. The average age of patients is 55 years, the youngest being 38, the oldest 68.

TECHNIQUE

The technique used is of the simplest kind and could be carried out in a doctor's surgery using ordinary aseptic precautions. The patient lies on the operating table, the scrotum is exposed, and the portion of the skin to be punctured is sterilized with either spirit or iodine. With a 20-ml. syringe and a size 2½-in. (6.3-cm.) 18 B.W.G. bored needle the hydrocele fluid is aspirated, the utmost care being taken that the point of the needle does not injure the testicle. When all the hydrocele fluid has been withdrawn the syringe is removed leaving the needle *in situ*, the greatest care being taken that the point of the needle remains within the hydrocele sac. 1-2 ml. quinine urethane (already loaded in a 2-ml. syringe) is then introduced and the needle withdrawn. In the majority of patients little or no pain is experienced. In sensitive patients a small weal of local anaesthesia is used where the needle is to be introduced.

The patient is again seen in a week or a fortnight's time. The local reaction varies in different patients. In some it has been necessary to aspirate when the reaction has been severe. In six patients it has been necessary to repeat the injections, in four patients the injection has been repeated twice. Patients are seen at intervals as required until the treatment has been completed. When the treat-

ment has been completed it is difficult to tell on which side the hydrocele has been, and there are no painful after-effects.

COMMENT

(1) Technique is simple and can be carried out in a doctor's surgery.

(2) Care must be taken that there is no underlying pathological condition of the testicle, such as tumour or tuberculosis or other infections. Until experience has been gained, or when in doubt, transillumination to find the most favourable spot for introducing the needle should be used.

(3) No time is lost from work, and there is no danger associated with the treatment if carefully carried out. The hydrocele fluid should be withdrawn slowly and gently. A plea is entered on behalf of the patient to avoid aspiration by the antiquated and painful method of using the trocar and cannula.

(4) A warning is given to avoid using too much sclerosing agent—for instance, 2 ml. need not be used where 1 ml. is considered sufficient. Sclerosing agents which give too much pain or severe reaction should not be used. Quinine urethane gives the best results.—I am, etc.,

Manor House Hospital, London, N.W.11. J. W. NICOLSON.

Hemiplegia in Young Adults

SIR,—Dr. G. Joly Dixon in his article entitled "Hemiplegia in Young Adults" (July 12, p. 53) calls attention to the frequency of strokes in this age group and to the obscurity of their aetiology.

It may be of interest to mention two cases recorded recently (Hawkins and Rewell, *Guy's Hospital Reports*, 95, Nos. 3 & 4) where massive haemorrhage of the brain took place in two healthy young adults. Both of these accidents were unheralded by any previous symptoms and were fatal. In one case hemiplegia was present shortly before death. These would have been labelled "idiopathic" had not sections been taken of the surrounding brain tissue, which appeared to the naked eye as quite normal. Microscopy showed that a haemangioma was present in each case to account for the cerebral catastrophe.

Such vascular anomalies are probably rare, but it seems possible that examination of sections of the surrounding brain in the fatal cases and arteriography in those that survive might demonstrate these lesions to be a more frequent cause of strokes in young people than is commonly believed.—I am, etc.,

Birmingham. C. F. HAWKINS.

Acute Non-specific Diarrhoea and Dysentery

SIR,—Having enjoyed a recent article on "Myth and Mumpsimus in Medicine" it was indeed a surprise to see another example which should be added to this collection. Dr. G. R. Kershaw (May 24, p. 717) has picked up an old seaman's belief and polished it up with technical language. He states that it is "a matter of common knowledge that *chilling of the abdomen* by the rapid ingestion of cold fluid in large quantities when the body is hot does often induce diarrhoea, and it is fairly well recognized that *chilling of the anterior abdominal wall* frequently does likewise." The first assumption is one with which many Americans, who experience extremely hot summers, evidently do not agree, as one may notice from the customary serving of iced water with meals and on other occasions. As for the second assumption, it is interesting to note the tradition of the cholera belt, the fear of leaving the abdomen exposed, and the shrinking from the open louvre in the Royal Navy, and the lack of evidence to show any ill effects from the cooling of the abdomen.

It is true that the latent heat of steam (or should it be of water?) is largely responsible for the cooling of the body. It should be noted, however, that this is much more effective in a dry climate than in a moist climate. In the Imperial Valley in California I have been informed that the humidity is very low, but that the temperature often keeps above 120° F. (49° C.) for weeks. One resident of this area said that the only way he and his neighbours could get to sleep before they constructed cooling devices was to wrap themselves in a sheet soaked in water. He claims that the wet sheet would evaporate in about half an hour, when the heat would be so great as to awaken him, and by repeating the process several times he would obtain a good night's sleep. I don't recall any history of diarrhoea, and yet the cooling effect would be much greater than from similar evaporation at sea.

In the Gulf of California on one trip in a Canadian Naval ship I had occasion to try an experiment with three willing subjects in the wardroom, who volunteered with me to sleep with the louvre exposed on our abdomens. Unfortunately the numbers were not sufficient to be of statistical significance, but although we experienced no diarrhoea we could not convince the other members that our action was other than folly.

The author of the article states that cooks "were from time to time victims of the outbreaks themselves," and that "cockroaches abounded at all times in the galleys and pantries." Surely one's knowledge of modern hygiene and the germ theory of disease would make one think carefully before suggesting a mechanical cause for a subsequent outbreak of diarrhoea, although as the Editor remarks in the annotation (p. 729): "any condition which lowers the resistance of the individual will favour the onset of infectious disease."

I will agree with Dr. Kershaw in his plea for experimental research. Surely this may be settled by some Naval medical officer in the Tropics who can divide his messes equally and study the effects of one group leaving the bare belly exposed to the evening miasma while the other group methodically buttons on the cholera belt.—I am, etc.,

Winnipeg. G. L. MORGAN SMITH.

Salaries of Specialists in N.H.S.

SIR,—I was perturbed recently to see that in the advertisement for specialists under the Iraq Government a different scale of remuneration was offered for psychiatrists and, I think, for radiologists. This was considerably less than that offered for surgeons and general physicians. It has occurred to me that there is a possibility that such a hierarchy of specialists, with the surgeons at the top and the lesser breeds at the base, might be contemplated for the new State medical scheme. If this is so then it would be a wise thing to state our objections to it at once.

I would claim that all specialists have the same responsibility and that if one is properly qualified he is worthy of remuneration equal to the others. It has always provided me with sardonic amusement how someone with half the experience and qualifications will jeer at one particular specialty—for example, psychiatry—without the appreciation that the work expended would have taken the specialist to the top of any other branch of medicine. It seems to me that the M.D. and the M.R.C.P. should be considered equal to the M.S. and the F.R.C.S., and if a D.P.M. is appended to the medical degrees it should not lead to poorer remuneration. If any branch of medicine is to be regarded as inferior, then this will lead to its neglect, and those who are suitably qualified will seek a more creditable type of work.

It would be interesting to know what other psychiatrists and radiologists think of this point of view. It seems to me to be of the utmost importance that this should be clarified before the scheme becomes solidified into law.—I am, etc.,

London, W.1. CLIFFORD ALLEN.

Medicine in the U.S.A.

SIR,—Having also spent 2½ years in an American medical school in Philadelphia I wish to associate myself wholeheartedly and in detail with everything Dr. N. K. Connolly says in his letter (July 19, p. 108). I would like to emphasize further just one point.

The teachers feel under the obligation to tell the students, in so far as they can, not only the name of the disease the patient is believed to be suffering from, but *what is going on in the patient's disordered body*. The emphasis is continuously on pathological physiology. When clinical signs have elucidated as far as possible the pathological anatomy, and the history provided guesses as to physiological changes, physiological methods are used to obtain further information. These methods are partly "clinical-"—such tests as circulation time and venous pressure—and partly biochemical—serum cholesterol and insulin tolerance. One hears the latter—biochemical—methods referred to—often scathingly—as "lab. tests." The extensive

application of these physiological and biochemical methods of investigation ("the excessive use of lab. tests") characterizes the *teaching* hospitals, and their use is to a considerable degree for teaching and research. In non-teaching hospitals as a rule these methods are resorted to only when their result is of immediate diagnostic or therapeutic import. It is, however, true that the American student feels the same academic interest in the serum cholesterol of an obvious "hyperthyroid" as does the English student in the rales of a patient whose skiagram shows undisputable signs of tuberculosis.

So much for American teaching practice. It will not be forgotten that the pioneers of these methods—Lewis, McKenzie, and others—worked in this country. Lewis's journal began publication nearly twenty years before its American counterpart. It is all the more pity to contrast our few, though distinguished, clinical scientists with the large influential group represented in the last *Proceedings* of the American Society for Clinical Investigation. It is certainly not that the *preclinical* teachers here fail to stress the physiological aspects of disease: it seems rather that contact between these departments and the wards and out-patient clinics is too slight. For some years now several American medical schools have followed the policy of sending registrars back to the physiology departments for more training, and then giving them posts part-time in the hospital and part-time in physiology. (An example of the fruits of such policy is Goldring and Chasis's *Hypertension and Hypertensive Disease*, Commonwealth Fund, 1944.) At the school at which I studied, the physiological department lectures on the eye were given by the professor of ophthalmology, and on the gastro-intestinal tract by a research worker in the gastro-intestinal clinic.

It may be argued by some that physiology has no business intruding into the art of medicine—they must be few nowadays; but those who feel for the possibilities of earlier diagnoses and more rational treatments should, so it seems to me, press for the widest possible exchange of British and American students and, more particularly, of men of registrar seniority.—I am, etc.,

Oxford. J. M. TANNER.

Holland's Example

SIR,—Last week I heard with admiration a quiet and dignified account, shorn of what must have been great suffering, of the steady and courageous resistance of over 80% of the Dutch medical profession to the overtures and aggressions of the German occupiers of their country—a resistance marked not only by courage but by professional rectitude and integrity. The result was that the Germans, then the conquerors of Holland and at the height of their military power, asked the Dutch medical profession on what terms they would resume their normal work. The terms given, the Germans did not again dare to interfere.

It was a sorry commentary on our lack of unity, but an inspiring example for our dealings with the Government with regard to the National Health Service. The "principles" upon which we have rested (and rested would appear to be the operative word) have not proved to be a clarion call to the profession at large, but I believe that we could be united upon certain articles of the terms of service. A firm front and we could dictate the remuneration; the hours at, and the days on, which we would hold surgeries; provision for holidays and time off during the week; adequate compensation, pension, and the like.

These are matters which require consultation and thought, but I would suggest that we insist on 28 days' leave and at least every other week-end off, the Government being responsible for providing a locumtenent; that no patient should be seen after 6 p.m. except in the case of accident or sudden emergency (and this without any reduction in remuneration which we decide is proper); and further that all expenses such as telephones, stationery, stamps, occasional drugs, etc., be refunded.

While it will be the duty of any member of the profession who joins the Service to put his best effort into the treatment of his patients, there is no onus on the profession to soften what will undoubedly appear to the public to be asperities in the Service. We have already too long borne, for instance, the inconvenience of the employer by seeing his employees at times not convenient to ourselves, and unless we take firm action now there is a danger that we shall descend from the honourable position of being servants of the public to that of being slaves of a system.—I am, etc.,

Ventnor, Isle of Wight. P. B. ATKINSON.

POINTS FROM LETTERS

Land of Excuses

Mr. A. WILFRID ADAMS, M.S. (Clifton, Bristol), writes: I have frequently stressed the dual responsibility for the present impasse in regard to the National Health Service. I admire Dr. G. C. Pether's forthright exposure, July 19 (p. 113), of the public's flagrant disregard for healthy living and his assertion that in effect the nation gets what it asks for. But is he as sound as he is pungent in disclaiming any responsibility on our side for what he deplores? Our consciences might have been clear had we kept the machinery of medical services bright and level with general advances in social progress. . . . Obvious reforms were long overdue in the spheres both of action and propaganda. (1) The medical curriculum grew out of all proportion to the utility of its contents in the doctor's daily practice, and increasingly neglected the art of medicine. (2) A medical fledgling on the day he qualified could put up his plate and start in full charge of patients. (3) Anyone could call himself a "specialist," and the title afforded the public no guarantee that it stood for what it should. (4) We accepted "on the panel" the Government's cheap valuation of a doctor. . . . (5) Many surgeries were dull, uncomfortable, and lacked a minimal hygienic standard. (6) Hospitals remained Victorian, gloomy, and situated in central urban sites. (7) Hospital services lagged behind commercial enterprise, were uncoordinated, and their resources were not pooled. (8) A Cancer Act was made law in 1939. The victims of this dreaded disease are still as numerous, arrive often too late for succour, and often are placed on a waiting-list. (9) A credulous and gullible public were left unshielded from exploitation by proprietary medicines and health foods and drink. The avenue trodden so boldly by the present revolutionaries in Parliament is lined by these memorials to our negligence. Admittedly we have some comfort in reflecting that the neglect of our collective responsibility is partly due to the signal devotion of the average doctor to the engrossing duties of personal medical services. By all means, as Dr. Pether exhorts them, let the *public* do a full 5½ days' week of worthy work, but let the *profession* also frankly admit that our influence might do much to rouse public interest in healthy living.

Nicotinic Acid Tolerance Test

Capt. A. ERDEI, R.A.M.C., writes: Dr. Z. A. Leitner (June 28, p. 945) wishes to have further particulars of the case of "artificial sprue" produced by massive doses of nicotinic acid, referred to in my letter (June 7, p. 822). The experiment was carried out under conditions when the liver functions were disturbed by an active amoebic hepatitis, and the B-vitamin biosynthesis and absorption were reduced by penicillin therapy and the irritation caused by emetine and E.B.I. Under the above conditions the nicotinic acid tolerance was determined twice daily; thus 1,800–2,000 mg. of the drug was given daily. After five days quite suddenly sprue-like symptoms set in. A typical "magenta-tongue" could be demonstrated to an assembled class, the mouth was sore, and the stools passed were bulky "white elephants." The symptoms gradually disappeared on the exhibition of 12 mg. riboflavine daily, in addition to thiamine and nicotinic acid, the latter in reduced doses. Maybe the case dramatically demonstrates the well-known fact that overdoses of one of the members of the B complex create a deficiency in the others, and that massive doses of nicotinic acid or thiamine wash out the liver's meagre reserves of riboflavine. The interesting result of the experiment seems to be that, while the so created sprue symptoms rapidly responded on riboflavine administration, this is unfortunately not the case with the real sprue. Rapid improvement can be noticed, however, in some cases on the exhibition of folic acid, another member of the heat-resistant B complex.

"Messages" in the N.H.S.

Dr. H. MAITLAND MOIR (Currie, Midlothian) writes: Dr. S. J. Hadfield's letter (July 19, p. 112) brings up a point which the G.P. will consider nearly as important as the payment under the N.H.S. —viz., can we insist on all "messages" being sent in by 10 a.m.? No, I fear we cannot. . . . Patients are careless enough at present, but when they know that they will be entitled to a "visit" whatever time of day the "message" is sent, many will not trouble themselves until well on in the day. I visualize a future when the G.P.'s work will never be done.

Signals for the Colour-blind

Dr. C. HOBART HOUGHTON (Umbogintwini, Natal) writes: As it appears that the most usual form of colour-blindness is in the difficulty of distinguishing between red, green, and yellow, would it not be better that in robots, etc., *blue* instead of *green* should be used for the "go ahead" signal? There must be many colour-blind persons driving motor-cars to-day.

Obituary

E. GUY DRU DRURY, M.D.

We announce with regret the death at the age of 75 of Dr. E. G. Dru Drury in Grahamstown, South Africa. Edward Guy Dru Drury was educated at University College and St. Bartholomew's Hospital, London. He took the conjoint qualification in 1896, and the London M.B., B.S. in the same year. In 1898 he proceeded M.D., and in 1908 he took the D.P.H. Dr. Drury had practised at Grahamstown since 1899. He was honorary secretary of the Cape of Good Hope Eastern Provincial Branch in 1906–9 and again in 1916–20. He was also at other times vice-president and president of that Branch, which he represented on the South African Committee in 1921, 1922, and 1924. He was president of the Cape Eastern Branch in 1931–2, and was elected a member of the South African Medical Council in 1933. He attended annual meetings of the B.M.A. as a representative in 1919, and again at the Centenary Meeting in 1932.

We announce with regret the death of Dr. JOSEPH HENRY WHITAKER, late medical superintendent of the Grove Hospital, Tooting. Dr. Whitaker received his medical education at Queen's College, Belfast, and qualified L.S.A. in 1897. He proceeded M.B., B.Ch., B.A.O. in 1895, and in 1898 took the D.P.H.Camb. In 1903 he took the M.D., R.U.I. He served as house-physician, junior house-surgeon, and casualty officer at the Royal Victoria Hospital, Belfast. Dr. Whitaker was appointed medical superintendent of the Grove Fever Hospital in 1920 and retired in 1935. He was, therefore, in charge of the hospital when it passed out of the hands of the Metropolitan Asylums Board and came under the administrative control of the London County Council. That this transformation took place with relative ease at the Grove Hospital was in no small part due to Dr. Whitaker's tact and kindly good humour. A medical superintendent inevitably suffers from being looked upon as being autocratically responsible for everything that goes right or wrong in the hospital under his control. This naturally tends to make him preoccupied with minor details and leads to an ultra-cautious approach to clinical problems; it tends to make the medical superintendent a careful administrator rather than an enthusiastic inspirer of a team of workers. Dr. Whitaker was not unaware of the difficulties of such a situation, and his good humour saved him from strife with his staff of medical officers, who will always have a kindly memory of him and of his hospitable nature.

Dr. KENNETH FRASER died at his home at Parbold, Lancs, on July 14 at the age of 74. A native of Inverness, he graduated M.B., Ch.B. at Aberdeen University in 1900, and then served for about a year as civil surgeon to the South African Field Force in the Boer War. In 1901 he published in the *Lancet* an account of a case of cocaine poisoning. On his return to this country he took the D.P.H. in 1903, and, after serving as Assistant Medical Officer of Health at Wigan, he was appointed Medical Officer of Health for Orrell, where he worked until his death. He also combined the duties of certifying factory surgeon with those of police surgeon to the Orrell section of the Lancashire Constabulary. From 1912 to 1933 he was consulting surgeon to the Wigan Infirmary. Dr. Fraser had been a member of the B.M.A. since 1912, and was elected president of the Wigan Division in 1930–1. He had been vice-chairman of the Wigan Panel Committee for some years and its chairman from October, 1946, though ill-health prevented his taking up the latter duty. Dr. Fraser married the elder daughter of the late Dr. Robert Hartley, of Pemberton, and we extend our sympathy to her in her loss.

Dr. D. H. DAVIES died on July 14 at the age of 61 at Porthcawl. David Henry Davies was educated at Cardiff and at the Middlesex Hospital, and qualified M.R.C.S., L.R.C.P. in 1912. He was honorary consultant surgeon to the Porth and District Hospital, and at one time house-surgeon to the Royal Infirmary, Cardiff. Dr. Davies was a native of Maesteg, and for some years had been in practice at Ynyshir and Wattstown. He retired eleven years ago on account of ill-health. Dr. Davies took an active interest in the St. John Ambulance Association, and for many years served as a justice of the peace at Porth and latterly at Bridgend.

Universities and Colleges

UNIVERSITY OF LEEDS

Cyril John Polson, M.D., F.R.C.P., Senior Lecturer in Pathology and pathologist to St. James's Hospital, Leeds, has been appointed to the first full-time Chair of Forensic Medicine in the University, and Cyril William Dixon, M.D., D.P.H., to the new post of Lecturer and Chief Assistant in Public Health.

UNIVERSITY OF EDINBURGH

At a Graduation Ceremonial held on July 16 the following medical degrees and diplomas were conferred:

M.D.—Louise F. W. Eickhoff, [1]R. O. Gillhespy, [1]L. S. Glass, [1]M. Hunter, M. S. Jones (awarded Medal for Thesis), [1]J. M. Kerr, [2]H. M. King, S. Lipetz, [1]R. M. S. McConaghey, [2]D. B. Peterkin, [2]J. A. Ross, J. N. Swanson, G. B. Tait, [1]E. R. C. Walker, A. W. Wright (Highly Commended for Thesis).

PH.D.—In the Faculty of Medicine: O. Olbrich, F.R.C.P.Ed.

M.B., CH.B.—Margaret Y. Abbey, R. MacG. Aitken, W. S. A. Allan, Beatrice M. Allen, Marjorie R. Allison, D. W. Anderson, E. Armitage, H. S. Bannerman, T. L. Barclay, M. A. Barnor, Mary S. S. Barr, Doris M. Beaton, K. W. Blaikie, Iris M. L. Bowman, R. A. Bremner, Margaret S. Brooks, Elizabeth L. Brown, I. F. Bruce, J. G. S. Buchanan, Anne M. Calder, C. W. A. Cameron, J. Campbell, Mary G. S. Campbell, Sheila H. Cattanach, Roma C. Cessford, Margaret M. Chalmers, J. A. L. Clark, Marianna I. H. Clark (*née* Goldmann), B. H. Colman, Janette G. Cowie, H. P. Croasdale, J. P. Crowdy, Jean M. Dance, Margaret S. Dawe, D. W. Dawson, J. G. Dickson, T. C. Dow, H. A. F. Dudley, Stella P. Eadie, P. N. Edmunds, E. Evans-Anfom, Peggy Everett, Doreen I. Falcy, R. S. C. Fergusson, J. Findlater, T. S. Forsyth, Marion G. Foster, T. Galla, J. M. Hagen, [2]Eileen V. Haldane (*née* McWilliam), F. Halliday, D. MacA. Hancock, Emma P. Harrison, Dinah C. M. Henderson, Elizabeth H. L. Henderson, Irene M. Henry, Patricia M. Hollis, A. Hordern, E. O. L. Hoskins, Margaret J. I. Howat, Mary Howson, J. Hughes, D. G. Hutchings, M. Hyman, C. W. G. Irvine, J. A. James, Isobel A. D. Jarvis, R. D. Johnstone, D. Keith, G. S. Kilpatrick, A. H. Kitchin, Dorothy I. Klein, Margaret J. Kyle, Grace J. Lang, P. M. Littlejohn, J. D. O. London, R. G. London, C. C. Lutton, J. M. McGillivray, W. T. Mackie, D. S. McLaren, R. S. Maclean, H. M. MacLeod, R. F. Mahler, Mary H. Marquis (*née* Potter), A. H. B. Masson, G. M. Maxwell, I. B. D. Middlemass, J. A. McC. Millar, R. A. Millar, Margaret E. Mowat, [2]A. R. Muir, Marion F. Muir, C. W. A. Murray, J. E. Murray, J. I. Murray Lawson, P. R. Myerscough, J. Newall, Dorinda E. M. Nixon, M. F. Oliver, D. W. Paterson, J. R. S. Paterson, S. L. Paton, Mary Patten, Annie M. Peach, E. C. Pink, T. B. Rankine, Muriel Richmond, H. D. Ritchie, J. M. Roberts, A. H. M. Ross, R. W. T. Ross, [1]L. F. W. Rowe, A. A. Sharp, D. Shearer, L. Simon, Sylvia R. Smith, N. T. Speirs, [2]Margaret Stirling, W. B. D. Storie, N. R. W. Taylor, W. J. Taylor, I. H. Thomson, J. N. Thorpe, Anne C. W. Walker, P. J. Walker, G. F. Watt, C. Weymes, C. B. Whittaker, J. D. Wilkie, J. G. A. S. Williamson, Janet P. Williamson, A. O. Wilson, S. G. F. Wilson, E. W. Wright, A. Yarrow.

A. F. J. Maloney, M.B., Ch.B., has been awarded second-class honours in pathology after graduation as B.Sc.

D.P.H.—[1]J. Borrowman, J. Dewar, R. G. Drummond, [1]W. A. Glen, [1]N. J. Graham, H. W. Horne, [1]J. K. Hunter, [1]D. P. Lambert, A. A. C. MacArthur, Lucy McFarlan, J. B. Menzies, R. Mitchell, [1]H. Pattinson, J. A. Petrie, P. W. R. Petrie, G. H. Scoular, J. H. Taylor, [1]R. Taylor, [1]W. C. Wightman.

D.T.M. & H.—B. G. H. Balfe, I. G. Cameron, J. W. Czekalowski, W. J. B. Darling, J. G. Davies, F. N. Macnamara, O. D. Macnamara, J. W. Martin, N. D. Paton, S. B. Roy, S. M. Shameem, H. B. Taylor, W. J. Toop.

D.M.R.—G. C. Griffiths, B. Hirschson.

D.I.H.—N. G. Douglas, J. D. Frame, E. I. B. Harvey, [1]G. H. McCracken, [1]D. Malcolm, [1]J. Millar, [1]J. Scott.

[1] *In absentia.* [2] Commended for thesis. [3] With honours.

The following scholarships, bursaries, prizes, etc., were awarded in the Faculty of Medicine: *Cameron Prize in Practical Therapeutics*, Prof. N. Hamilton Fairley, M.D., F.R.S., F.R.C.P. *Ettles Scholarship and Leslie Medal, Scottish Association for Medical Education of Women Prize, Buchanan Scholarship in Obstetrics and Gynaecology, and Dorothy Gilfillan Memorial Prize*, Eileen V. Haldane. *Vans Dunlop Scholarship in Clinical Therapeutics and Public Health, and Wightman Prize in Clinical Medicine*, A. H. Kitchin. *Murchison Memorial Scholarship in Clinical Medicine*, Constance C. Forsyth. *Ellis Prize in Physiology*, Helen N. Duke. *Mouat Scholarship in the Practice of Physic*, J. Newall. *James Scott Scholarship in Obstetrics and Gynaecology*, Margaret Stirling. *Beaney Prize in Anatomy and Surgery, Keith Memorial Prize in Systematic Surgery, and Pattison Prize in Clinical Surgery*, H. A. F. Dudley. *Annandale Medal in Clinical Surgery*, Mary S. S. Barr. *Murdoch Brown Medal in Clinical Medicine*, A. O. Wilson. *Royal Victoria Hospital Tuberculosis Trust Medal*, A. H. B. Masson. *Sir Robert Jones Prize in Orthopaedic Surgery*, R. B. Duthie. *Lawson Gifford Prize in Obstetrics and Gynaecology*, D. W. Paterson. *Stirton Bursary and Colonel Thomas Biggam Memorial Medal and Prize in Pathology*, W. F. Coulson. *Wellcome Medal and Prize in the History of Medicine*, G. M. Wilson. *Prox. Acc.*, L. H. Berman.

UNIVERSITY OF WALES

At a Congregation held on July 15 the honorary degree of LL.D. was conferred on Sir Ewen J. Maclean, M.D., F.R.C.P., F.R.C.O.G., Emeritus Professor of Obstetrics and Gynaecology in the Welsh National School of Medicine and Past-President of the British Medical Association and the Royal College of Obstetricians and Gynaecologists, for his contribution to the development of medical education in Wales, and on David Llewelyn Williams, C.B.E., *M.C.*, F.R.C.S.Ed., member of the Court of the University of Wales and formerly medical officer of health for the County of Denbigh, for his contribution to the development of public health services in Wales.

The Minister of Health has investigated the supply of surgical rubber gloves, and announces that control cannot be ended. The Central Medical War Committee will deal with all applications, including supplementary applications, by medical practitioners in private practice for certificates to purchase rubber gloves.

Medical Notes in Parliament

In the House of Lords on July 18 the Royal Assent was signified to the Penicillin Act, the National Service Act, and the Indian Independence Act.

Regional Hospital Boards

Mr. BEVAN stated in reply to Col. Stoddart-Scott on July 18 that the following Members of the House of Commons had been appointed to Regional Hospital Boards: N.W. Metropolitan, Mr. F. Messer (Tottenham, South) as Chairman, Dr. S. J. L. Taylor (Barnet) as member; N.E. Metropolitan, Mr. H. W. Butler (Hackney, South), Dr. L. Comyns (Silvertown), Dr. Somerville Hastings (Barking) as members; S.W. Metropolitan, Mr. R. Sargood (Bermondsey, West) as member.

Unstable Adolescent Girl

Mr. PLATTS-MILLS inquired on July 24 whether Mr. Chuter Ede had considered the Report by a Joint Committee of the British Medical Association and the Magistrates' Association on the problem of the unstable adolescent girl, and if he proposed to give effect to any of the recommendations made in that Report.

Mr. EDE replied that a copy of the report reached his Department in the previous week. The recommendations made would receive consideration, but he could not yet say what action might be taken on them.

Visiting Service Patients

Mr. BELLENGER said that hitherto arrangements for sending a relative to see a Service patient on the dangerously ill list in a military hospital where such a visit was expected to assist recovery had been limited to Europe. It had now been decided to extend the scheme to all overseas stations of the Services, with the exception of one or two small stations which a relative could not reach within any reasonable time. He doubted, however, whether the scheme would, for practical reasons, operate for any of the more distant stations.

Closure of Maternity Homes

Mr. MEDLAND on July 24 asked Mr. Bevan to state the number of maternity homes that had had to be closed in the past six months owing to an obscure infectious sickness among babies and mothers.

Mr. BEVAN answered that he had been notified of the temporary closure of seven maternity homes or hospitals in the last six months because of outbreaks of gastro-enteritis, which he assumed to be the sickness to which Mr. Medland referred. The causal agents of some of these outbreaks were known, but there was still a type of diarrhoeal disease in very young infants that had so far remained unsolved. Active research was being pursued in this field.

Botulism and Canned Vegetables

Mr. JANNER on July 24 asked if the attention of Mr. Bevan had been called to the evidence of a pathologist at an inquest on July 16 to the effect that his Department opposed the tinning of vegetables on the ground that it was dangerous.

Mr. BEVAN replied that he had seen Press reports indicating that the pathologist's statement, which misrepresented the Ministry's views, was later corrected by his own explanation that he was referring only to home-canned vegetables. The real position was that there might be a risk of botulism from home-canned or home-bottled vegetables because the high steam pressure needed to ensure complete sterility during the canning process could not ordinarily be applied in the home. Even this slight risk did not arise with home-canned or home-bottled fruit, because of its acid content, nor with beans preserved in salt. With commercially canned vegetables there had never been a reported case of botulism in this country, and the risk was considered negligible.

Questioned on the same subject on July 1, Mr. HERBERT MORRISON said that this was not a matter for research at the present time, the relevant facts being already well known. The risk was practically confined to foods preserved without due regard to the precautions officially recommended.

Workers from Europe.—Of 5,283 female European volunteer workers brought to this country 2,694 have been placed in hospitals and sanatoria. Permits have also been issued from May last year for the employment of other foreign domestic workers in hospitals and similar institutions.

National Service.—Men called up for national service during the first six months of 1947 numbered 100,000.

Corsets.—Supplies of cloth to manufacture corsets that are ordered through a medical prescription have improved considerably and the Ministry of Supply is doing its utmost to see that this improvement is maintained.

Vaccine Lymph.—For the manufacture of vaccine lymph the Lister Institute prefers sheep to calves because they are more readily obtainable, easier to keep clean, hardier, and not subject to tuberculosis, though post-mortem examination of every animal used eliminated the latter risk when calves were used.

Payment for Lymph.—Payment to the Lister Institute for vaccine lymph supplied by the Institute for the purpose of public vaccinations is £10,000 a year up to a total of 500,000 doses annually, with a payment of twopence per dose for any supply additional to this.

Rye Biscuits.—In very special cases, on medical certificate, "Points" are given in exchange for bread units where Mr. Strachey's medical advisers agree that rye biscuits are essential. Because supplies are limited he cannot leave the decision to local food offices.

Mentally Deficient.—On Jan. 1, 3,898 persons who had been reported as mentally deficient awaited admission to an institution for treatment. During 1946 the number of children of school age reported as mentally deficient under Section 57 of the Education Act, 1944, was 4,209.

Infantile Paralysis.—During the 26 weeks ending June 28, 1947, 398 cases of infantile paralysis were notified in England and Wales. The comparable figure for 1939 is 239.

Venereal Disease.—Mr. Bellenger proposed to visit the Rhine Army during the Recess and will take the opportunity to discuss with the authorities on the spot the ways by which the high incidence of venereal disease may be reduced, and also other problems.

German Doctors.—Mr. Ernest Bevin gave an assurance on July 23 that no German doctors or surgeons whose medical services were urgently needed in the British Zone were prevented from resuming practice because of their former connexion with the National Socialist Party.

Coal Board Medical Staff.—Nine medical officers, Mr. Shinwell stated on July 23, are employed by the Ministry of Fuel and Power, at headquarters and in the coalfields, on inspectorial and advisory duties as regards first-aid and occupational diseases at coal mines, metalliferous mines, and quarries. The National Coal Board was in process of recruiting a medical staff comprising one Chief Medical Officer at headquarters, who had already been appointed, and seven medical officers for duty in the coalfields. These appointments were being made in pursuance of the Board's intention to develop and co-ordinate, nationally and regionally, an industrial medical service of the highest possible standard. At coal mines the service would be associated with medical treatment centres equipped on modern lines and in charge of fully qualified nurses and supervised part-time by doctors. To date, over 20 had been appointed. The number would be increased as accommodation could be built and trained staff became available.

Atomic Energy.—Mr. Wilmot announced on July 23 that an atomic energy plant would be established at Sellafield, West Cumberland. Later, on July 24, Mr. Wilmot said that the work at the research station at Harwell, Berks, was making good progress, and the first experimental pile would be in operation later this year. The Government hoped to build up at Harwell a university of nuclear physics second to none in the world.

Atomic Effluents.—Answering Mr. Harold Davies on July 23, Mr. Wilmot said the Medical Research Council and officers of the Ministry of Supply were engaged on research into the possible effects on rivers of effluents from atomic energy factories. The General Medical Council's special committee under Sir Henry Dale considered that the factory at Sellafield would have no ill effects upon the health of the people in the locality.

The Services

DEATHS IN THE MEDICAL SERVICES

Acting Squadron-Leader HUMPHREY FRANCIS WARREN FRY was killed on July 10, as the result of a road accident. Squadron-Leader Fry was born in January, 1922, and studied medicine at Queen's University, Belfast, where he qualified M.B., B.Ch. in 1945. After holding a house appointment at Royal Victoria Hospital, Belfast, he was appointed to a commission as flying officer in the Medical Branch of the R.A.F.V.R. on Nov. 1, 1945. At the date of his death Squadron-Leader Fry was serving as a medical officer at an R.A.F. headquarters overseas.

No. 28

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended July 12.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1947					1946 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	67	1	18	1	—	33	4	17	—	1
Deaths		—	—				—	1		
Diphtheria	181	25	40	10	11	277	30	71	34	15
Deaths	2		—	—	—	2	—	1	—	—
Dysentery	50	4	15	—	—	61	10	23	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	2	—	—	—	—	5	—	—	—	—
Deaths		1					—			
Erysipelas			25	9	1			30	3	1
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				52					64	
Deaths	82	6	4	9	2	39	4	9	12	3
Measles*	9,133	473	54	172	8	3,981	630	267	54	5
Deaths	5	—	1	1	—	2	—	—	—	—
Ophthalmia neonatorum	82	7	23	—	—	69	2	11	—	—
Deaths										
Paratyphoid fever	8	—	1(A) 2(B)	—	—	17	—	1(B)	1(B)	—
Deaths	—	—	—	—	—	1	—	—	—	—
Pneumonia, influenzal	332	31	5	1	2	416	29	4	1	1
Deaths (from influenza)†	3	—	1	—	—	5	1	1	1	—
Pneumonia, primary			123	9				127	12	
Deaths		19		7	9		26		9	6
Polio-encephalitis, acute	16	6				—	—			
Deaths		—					—			
Poliomyelitis, acute	110	9	7	8	—	12	—	—	4	—
Deaths		2					—			
Puerperal fever		1	18		—		—	15		—
Deaths										
Puerperal pyrexia‡	115	9	10	—	3	149	9	6	—	1
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	918	95	114	39	33	845	72	112	21	23
Deaths	—	—	—	—	—	—	—	—	—	—
Smallpox	3	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	12	1	2	2	8	6	—	5	6	—
Deaths	—	—	—	—	—	1	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	2,000	267	42	56	15	2,270	148	28	36	14
Deaths	7	—	2	4	—	12	2	2	—	—
Deaths (0–1 year)	340	33	66	23	12	334	52	56	35	10
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	3,730	563	540	171	101	4,003	604	514	181	103
Annual death rate (per 1,000 persons living)			11·2	10·8				11·3	11·6	
Live births	9,327	1468	1156	434	231	8,546	1316	987	338	228
Annual rate per 1,000 persons living			23·3	27·4				19·9	21·7	
Stillbirths	219	31	38			215	18	37		
Rate per 1,000 total births (including stillborn)			32					36		

*Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

†Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

‡Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Poliomyelitis

The seasonal rise started about six weeks earlier than usual this year, and the notifications during the week ending July 12 exceeded any weekly total of recent years. A large increase occurred in the following week, when the notifications rose from 110 to 177. The last two large outbreaks of poliomyelitis were in 1926 and 1938, when 1,160 and 1,462 cases were notified during the year. The largest weekly totals were 78 in the 23rd week of 1926 and 81 in the 32nd and in the 42nd weeks of 1938. A bi-modal curve—a late summer peak and another peak in October—has been a feature of the incidence of this disease, and it seems likely that an unusually large number of cases will occur this year. A comparison of the trends in the present and the two previous large outbreaks is interesting.

Number of Notifications

Week	1926	1938	1947	Week	1926	1938
22	2	5	3	38	41	60
23	8	5	22	39	65	56
24	9	—	31	40	46	65
25	10	4	44	41	62	77
26	3	3	56	42	68	81
27	5	6	79	43	78	70
28	8	8	110	44	36	70
29	16	19	177	45	29	51
30	25	41		46	47	45
31	20	61		47	55	39
32	37	81		48	41	37
33	47	77		49	37	27
34	40	71		50	25	31
35	41	73		51	23	29
36	53	73		52	14	16
37	75	76				

During the week ending July 12 the disease was widespread, and the 110 notifications involved 24 counties. The largest return was that of Yorkshire West Riding with 26 notifications from 19 registration areas (Bradford C.B. 4). The largest local outbreak was Dorsetshire, Wareham and Purbeck R.D. 8. During the week ending July 19 the 177 notifications involved 34 counties. The largest of the local centres of infection were Surrey, Croydon C.B. 7; Warwickshire, Birmingham C.B. 7; Cheshire, Runcorn R.D. 6; London, Wandsworth 5; Northumberland, Newcastle-upon-Tyne C.B. 5.

This most recent total of 177 is the highest figure recorded since compulsory notification was introduced in 1912, and it is feared that the incidence in the past week has been still higher and that the peak figure has not yet been reached.

Cases were widely scattered over these different counties in the week ending July 19. The overall picture is therefore one of a large number of outbreaks, sometimes spreading a little locally, rather than of an epidemic spreading from one centre. The number of notifications rises regularly every year at about this time, but this year the rise came early and has been more rapid than ever before. It should be remembered that in the past we have never suffered the severe epidemics which have been experienced in some other countries. The highest figure recorded in England and Wales between 1912 and 1946 was 85 (uncorrected), shown in the table as 81 (corrected) in the week ending October 22, 1938. Since July 1 there have been 135 patients suspected of suffering from poliomyelitis admitted to L.C.C. hospitals, but many of these failed to develop paralysis. Since July 22 the admissions have ranged between 7 and 16 a day; 8 cases were admitted on July 28.

The spread of the disease is difficult to control, because for every case with obvious signs there are many more with a mild and indefinite illness. There are also perfectly healthy carriers who cannot be recognized by any practicable method. The essential principles in control are therefore to secure the segregation of suspicious cases of illness occurring in the contacts of a definite case, and to limit the aggregation of susceptible persons. The exact application of measures to this end must be a matter for the discretion of the medical officer of health.

It is theoretically possible that infected food and drink may be vehicles of dissemination of the virus and that flies may play a part, and preventive action against these possibilities is also advocated. The present widespread distribution of cases in this country does not, however, suggest any dissemination by food or water, and little evidence exists that this method of dissemination has ever been important elsewhere in the world. All these matters were discussed in a memorandum addressed to the medical profession which appeared in the *Journal* of July 26 at page 141.

This memorandum also included a request to the medical profession to send pathological specimens for the purposes of research to the Central Public Health Laboratory, Colindale Avenue, London, N.W.9 (Telephone: Colindale 6041).

American Experience

While Britain looks like having for the first time an "American experience" of poliomyelitis the U.S.A. has fewer cases at present than for many years past. So far over the whole country only 1,000 cases have been reported, as compared with some 2,000 at this time last year. In 1946 there were altogether 25,000 cases in the U.S.A. Towards the end of last summer in the cities of Minneapolis and St. Paul something akin to martial law was introduced. All big gatherings were banned. Cinemas and theatres were closed, and children were kept indoors. The town of Rockford, Illinois, was dusted throughout with D.D.T. powder, and a Press and poster campaign advised everyone to avoid over-exertion, not to swim in very cold water, and to keep flies away from food. In general, American observers find that 50% of cases recover completely, 20% suffer a slight but not severe handicap in later life, 25% are crippled, and in 5% of cases the disease proves fatal.

One of the notable American epidemics was in 1916, when in New York, for example, there were 9,023 notifications in a population of about 5½ million. In England and Wales in 1938 there were 1,489 notifications in a population of about 41 million. The highest weekly figure for New York in 1916 was 1,200 notifications, as against our latest figure of 177 for the whole of England and Wales.

Long-range Tests of B.C.G.

Vaccination with B.C.G. is now being tested in a long-range controlled programme arranged by the United States Public Health Service at Columbus, in the State of Georgia. Public health service physicians have tested some 16,000 children in the 47 schools of Muscogee County, where the City of Columbus is located. Those children who showed no immunity were vaccinated. After about six months the tests will be repeated. Those who again show no immunity will be vaccinated once more, and the process will be repeated until immunity has been established. Then for several years these children will be watched and tested, and precise statistics will be collected.

Over a long period of years it is hoped to measure variations in reaction, to fix the dose of B.C.G. which should be given, and to establish the degree and persistence of immunity. Also of importance is the establishment of dependable standards for manufacture of the vaccine. Support for the Georgia tests came from the recent conference on B.C.G. vaccine, conducted by the tuberculosis control division of the United States Public Health Service at Bethesda, Maryland, near Washington, D.C. This conference recommended, among other things, "that the tuberculosis control division set up a controlled study in a community with a population of 100,000 or more, to determine immediate and long-range results" of B.C.G. vaccination.

Dr. Herman E. Hilleboe, representing the United States Public Health Service, reviewed past experience with vaccination. Several million vaccinations have been performed since the first work with human beings was done by Calmette and Guérin in 1921, but B.C.G. vaccination has not been widely accepted in the United States.

Dr. Joseph B. Aronson, of Philadelphia, reported to the conference on B.C.G. studies of the American Indian. At the age of 20, he said, "100% of the Indian population has tuberculosis, in contrast to a lower proportion in the coloured and a much lower proportion in white population groups." He told of a study begun in 1935 of 3,000 persons, aged 1 to 20, who were selected from a larger group on the basis of a negative tuberculin reaction. These persons were given annual tuberculin tests and chest *x*-ray examinations for six years, and the results indicated that the B.C.G. vaccine reduced the incidence of tuberculosis. This evidence, however, was not considered sufficient to recommend general vaccination by all physicians in the country. The public health service in its report of the conference said:

"After a detailed review of the literature and the presentation of papers by the members of the conference, it was concluded that B.C.G. vaccination appears to confer increased resistance to tuberculosis for the period covered in the studies. At present, however, information is incomplete as to the amount of this resistance or its duration. Furthermore, these studies as yet do not answer the question of the long-term effect of B.C.G. vaccination on ageing members of the population."

The conference concluded, however, that "there have been no proved cases of progressive disease from B.C.G. vaccination in human beings," therefore continued study by means of larger control groups was recommended. It was also recommended that conferences be held with representatives of European, South American, and Asiatic countries in order to work out plans for uniform methods of producing B.C.G. vaccine, and to make a comparison of the vaccine strains used in various countries of the world.

Smallpox

There have been no confirmed notifications of smallpox during the past week. The disease was suspected in a member of the Polish Resettlement Corps who entered England from Holland on July 10 and was removed to hospital at Aldershot on July 17. It is now known that this man was not suffering from smallpox. The 16-day period of surveillance of the contacts of the last cases at Willenhall, Barnsley, and Bilston has now expired without further incident, and the position is not unsatisfactory. There is a reasonable chance that the country is once again free from smallpox.

Food Poisoning

In the outbreak of food poisoning at Twyford, near Winchester, reported in these columns on July 19 (p. 117), out of sixteen people who attended a luncheon party on July 12 fourteen suffered from symptoms suggestive of bacterial food poisoning. Examination of the faeces of residents and domestic staff revealed symptomless carriers of *Salmonella typhi-murium*, and this organism was isolated from the stools of one of the patients.

Discussion of Table

In *England and Wales* infectious diseases were less prevalent during the week. There were decreases in the incidence of measles, 1,136, whooping-cough 240, and scarlet fever 48; the only rise was in the notifications of acute poliomyelitis 31.

The largest declines in the incidence of measles were Yorkshire West Riding 262, Warwickshire 162, Glamorganshire 130, Surrey 99, and Sussex 44, while the largest rises were Gloucestershire 87 and Cambridgeshire 85. The only variation of any size in the local returns of scarlet fever was a decrease of 23 in Lancashire. A small decrease in the incidence of whooping-cough occurred in most areas; the largest fall was 58 in Lancashire.

The returns of diphtheria and dysentery did not show any appreciable differences from those of the preceding week. The three cases of smallpox were notified from Staffordshire, Willenhall R.D. 1, and Yorkshire West Riding, Barnsley C.B. 2.

In *Scotland* a decreased incidence was reported for acute primary pneumonia 36, measles 14, and scarlet fever 12. There were 7 cases of poliomyelitis: Glasgow 4, Ayr County 2, and Kilmarnock 1.

In *Eire* infectious diseases were less prevalent, and there were falls in the notifications of whooping-cough 48, measles 14, scarlet fever 8, and diphtheria 5. The incidence of diarrhoea and enteritis has not changed appreciably during the past three weeks; the notifications were 56, 54, and 52 for the whole country and 46, 37, and 41 for Dublin C.B.

In *Northern Ireland* the chief feature of the returns was a fall in the notifications of typhoid from 17 to 8 (Belfast C.B. 7 and Armagh R.D. 1).

Week Ending July 19

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,036, whooping-cough 1,931, diphtheria 202, measles 8,400, acute pneumonia 306, cerebrospinal fever 60, acute poliomyelitis 177, acute polioencephalitis 16, dysentery 56, paratyphoid 12, typhoid 10. One case of smallpox was imported during the week.

Medical News

Medical Women's Federation

The London Association of the Medical Women's Federation requests nominations for president and four ordinary members of the executive committee. Nominations duly proposed and seconded, the consent of the nominee having been obtained, should reach the Hon. Secretary, 7, Wimpole Street, London, W.1, not later than first post on Aug. 8.

Quinine no longer Controlled

The supply of quinine and its salts, and other products of cinchona bark, is now satisfactory, and an order revoking their control has therefore been made. For the time being export control will be retained on quinine, quinidine, cinchona, and other salts, to ensure that the relatively small quantities of these drugs needed for essential purposes are available in the unlikely event of a future shortage.

Lady Watson

The Secretary of State for Scotland has appointed Lady Watson, M.B., Ch.B., to be a member of the Board of Trustees for the National Galleries of Scotland until March 31, 1952.

Royal Society Reception

The Fellows of the Royal Society held a reception at Burlington House, Piccadiily, on July 17, on the occasion of the celebrations of the centenary of the Chemical Society and of the meeting of the International Congress of Pure and Applied Chemistry. Sir Robert Robinson, P.R.S., received the guests, who included delegates from some 25 nations.

In Memory of W. A. Cochrane, F.R.C.S.Ed.

The Earl of Home unveiled a plaque in memory of William Alexander Cochrane, F.R.C.S.Ed., at the Princess Margaret Rose Hospital for Crippled Children at Fairmilehead recently, in recognition of his outstanding services to the hospital and to the development of orthopaedic surgery. Mr. Cochrane was the first surgeon in charge of the hospital from 1930 to 1944.

Leprosy Film

A film on the control of leprosy has been made by Mr. John Page in Nigeria, where the Government is carrying on a campaign against the disease with the help of the native administration and the missions. Mr. Page expects to be there for another four or five months to complete other films.

COMING EVENTS

Medical Society of the L.C.C. Service

A clinical meeting of the Medical Society of the L.C.C. Service will be held at the Northern Hospital, Winchmore Hill, N., on Thursday, Aug. 7, at 2.30 p.m.

Franco-Anglo-American Medical Society

The third quarterly meeting of the Franco-Anglo-American Medical Society (British Section) will be held at 11, Chandos Street, W., on Tuesday, Aug. 12, at 2.30 p.m., when there will be a discussion on the "Four-year Health-first Organization" research programme on nature resources inherent in climate and soil from North-west Scotland to South-east France. The meeting is open to the lay public as well as to members of the medical profession. The acting honorary secretary of the society is Dr. F. Aylmer Hort, 6, Cavendish Avenue, St. John's Wood, London, N.W.8.

American Public Health

The 75th annual meeting of the American Public Health Association (1790, Broadway, New York, 19) will be held at Atlantic City, New Jersey, from Oct. 6 to 10. The association will be assisted in the celebrations by numerous other American organizations. Exhibits and the scientific programme will describe progress in public health over the last 75 years.

French Medical Congress

The Association des Médecins de Langue Française will hold a congress at the Paris Medical Faculty on Oct. 16–18. Prof. A. Lemierre will preside. There will be discussions on genetics, antihistamine compounds, and pulmonary cysts. Further particulars may be obtained from M. Georges Masson, 120, Boulevard St. Germain, Paris VIe.

Chilean Conference on Obstetrics

The Society of Obstetricians and Gynaecologists of Chile will hold a meeting from Nov. 30 onwards at the University of Chile, Santiago. Those intending to take part may be enrolled as associate members for 300 pesos or the equivalent in foreign currency. Papers may be sent to the conference or read in person; they should reach the Society by the end of October.

BIRTHS, MARRIAGES, AND DEATHS

The charge for an insertion under this head is 10s. 6d. *for* 18 *words or less. Extra words* 3s. 6d. *for each six or less. Payment should be forwarded with the notice, authenticated by the name and permanent address of the sender, and should reach the Advertisement Manager not later than first post Monday morning.*

BIRTHS

LANGHAM-HOBART.—On July 3, 1947, at Newcastle-on-Tyne, to Jean Langham-Hobart, M.B., Ch.B. (*née* Terry Thomas), wife of Neville C. Langham-Hobart, a daughter.

OGILVIE.—On July 21, 1947, at 39, Hatchlands Road, Redhill, to Jean (*née* Torrens), wife of Dr. J. P. H. Ogilvie, a daughter—Patricia.

O'MAHONY.—On July 5, 1947, at London, to Rosaleen (*née* McLaughlin) and Dr. John B. O'Mahony, Clunmuire House, Killorglin, Kerry, Eire, a daughter—Sheilagh Ann Deidre.

STOCKINGS.—On July 16, 1947, at 295, Brownhill Road, Catford, London, to Enid Marjorie, wife of Dr. G. Tayleur Stockings, a son—Adrian Peter.

MARRIAGE

ROSSER-DASH.—On July 21, 1947, at Berkeley, Gloucestershire, Brinley Mervyn Rosser to Peggy Mildred Dash, M.B., B.S.

DEATH

MUMMERY.—On July 20, 1947, at Jersey, Channel Islands, Norman Howard Mummery, M.R.C.S., L.R.C.P. First Chairman of the Association of Industrial Medical Officers, husband of Isabel Mummery, aged 70 years.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Cure of Morphine Addiction

Q.—*A confirmed morphine addict aged 60 has asked for treatment to enable him to discontinue the drug. Is there a satisfactory cure?*

A.—It is impossible to answer such a question in a mere paragraph. It can be said, however, that treatment must be institutional, otherwise there is not the slightest hope of even short benefit. Secondly, a three-months residence is the minimum desirable. Thirdly, a relapse is highly probable. If the patient is a doctor the prognosis in this respect is extremely bad. The principles of treatment are withdrawal of drug, substitution of non-habit-forming sedatives, and physical and mental re-education.

Removal of Placenta

Q.—*Is there any method, short of manual removal, which can be adopted in a case of retained placenta which cannot be expressed by squeezing the uterus? What is the technique of injecting saline into the umbilical vein?*

A.—It is assumed that the question is concerned with a placenta which is still wholly or partly attached to the uterus, and not one which is separated and lying in the lower uterine segment or vagina. Injecting the cord with saline is a time-consuming method and is applicable only when the condition is not complicated by haemorrhage. The technique is simple: after painting the cord with antiseptic a needle is inserted into the vein and up to 400 ml. of sterile saline is injected by means of a large-size syringe. The idea is to increase the bulk of the placenta and to bring about its separation by distending the villi and by causing a disparity between the size of the placenta and its site. The injection can be followed by Credé's manœuvre. An alternative treatment sometimes carried out is to cut the cord and to bleed the placenta to reduce its bulk. In either case the results are uncertain.

This question rather implies that manual removal of the placenta should be carried out as a last resort and only when all else has failed. Views on this matter are changing rapidly, and it is becoming recognized that the danger of manual removal lies in carrying it out too late when the patient is already exsanguinated or in a state of shock. If performed promptly and while the patient is in good condition it carries less risk than repeated squeezing of the uterus. Indeed, Credé's method is dangerous and is fast losing favour.

Finally, there is the modern treatment whereby ergometrine (0.5 mg.) is given intravenously. Under hospital conditions the results are very satisfactory, and in some clinics it is becoming a routine procedure in the management of the third stage of labour. Usually it produces immediate separation of the placenta, which can be expressed. If, however, the placenta does not come away at once, manual removal has to be carried out without delay. There is still considerable discussion as to whether this treatment is advisable in domiciliary midwifery, either as a routine or when the placenta is retained without haemorrhage. If there is third-stage bleeding, however, then, irrespective of working conditions, an intravenous injection of ergometrine is preferable to repeated attempts (and some would say even a single attempt) at Credé's manœuvre. Even if an hour-glass contraction should result it can be dealt with at leisure once the haemorrhage is controlled.

Urethane

Q.—*What are the local and general anaesthetic properties of urethane?*

A.—Urethane is not known to have any local anaesthetic action. Its general anaesthetic properties are much feebler in man than in animals, but even in animals large doses are

required—not less than 1.5 g. per kilo, which corresponds to 90 g., or more than 3 oz., for a man. This is given by injection of a solution, and, since it is not easy to prepare a solution stronger than 25%, the volume to be injected into a man would be 12 oz., assuming that man was as sensitive as an animal (a rabbit, for example). Urethane is not used even in animals when recovery from the anaesthetic is intended.

Penicillin in Chronic Cystitis

Q.—Would penicillin be of help in a man aged 75, not fit for operation, suffering from chronic cystitis? If so, in what dosage? There is no obstruction to the outflow of urine.

A.—This question cannot be answered on the meagre information given. Whether penicillin would be beneficial depends first on the organism responsible for the cystitis, and secondly on whether there is any condition in the genito-urinary tract which prevents its clearing up—residual urine, a small calculus or diverticulum, infected kidneys, etc. Penicillin is of little help in the commonest form of urinary infection—namely, with a coliform bacillus. If the infection is a mixed one and some of the organisms are penicillin-sensitive, these organisms are likely to disappear after treatment, but the remainder may multiply, so that the final condition of the patient is but little better. Penicillin should not be given blindly.

Trusses

Q.—A heavily built, moderately active man aged 70 has right scrotal and left inguinal herniae, both self-reducing. Is there an alternative form of control to the rather cumbersome steel spring truss? An appliance with rubber pads and a webbing belt used to be made; would this be satisfactory, and, if so, is it still obtainable?

A.—Generally speaking the comfort of a truss is inversely proportional to its efficiency, and if by "heavily built" is meant fat it is unlikely that any appliance not based on a steel spring will be satisfactory. Much, however, depends on (*a*) the condition of the patient's musculature, (*b*) the size of his external abdominal rings, and (*c*) the amount of strain involved in his "moderate activity." The rubber-pad truss is still obtainable, but is best suited to the bubonocele type of hernia. As an alternative to the "cumbersome steel spring truss" the vulcanite washable spring truss might be tried. This is malleable and can therefore be fitted to the individual, hence avoiding the need for perineal straps; also it is very light.

Treatment of Oculogyric Crises

Q.—What is the best treatment for paralysis agitans with severe eye spasms? Hyoscine, pethidine, and ergotamine tartrate, separately, have been tried without result.

A.—The eye spasms are probably oculogyric crises, in which the eyeballs involuntarily deviate in one direction, usually upwards, for a matter of minutes or maybe hours. The best remedy in such an event is amphetamine, 5 to 15 mg. Previous to the employment of this drug it was usual to get the patient to lie down with eyes bandaged and to take phenobarbitone gr. 1–2 (65–130 mg.). Amphetamine usually proves more efficacious.

Estimation of Uric Acid

Q.—What is the benefit of estimating plasma uric acid in place of blood uric acid? Is 6 mg. considered normal for plasma?

A.—Subject to the conditions imposed by the permeability of the capillary endothelium, plasma constituents are in equilibrium with the tissue fluid; plasma concentrations are therefore likely to give a better indication of the cell environment. Transudates and exudates have approximately the same uric acid concentration as plasma. It has been claimed that the analysis of plasma enables a more precise differentiation to be made between gouty and non-gouty individuals. The blood of normal fasting human beings contains 3 ± 1 mg. per 100 ml. of free uric acid, of which the largest fraction is in the plasma (cells 2 ± 1 mg.; plasma 4 ± 1 mg.). The figure of 6 mg. should be regarded as reaching the highest limit of normality.

NOTES AND COMMENTS

Loa loa Infection.—Dr. J. R. H. PASQUAL (Barakin Ladi, Nigeria) writes: The extraction of filaria loa during its subconjunctival passage across the eye is a comparatively simple procedure. Yet the methods commonly employed result in a high percentage of failures, due to the escape of the worm before local anaesthesia is complete or to its concealment behind an inflamed and chemotic conjunctiva. As a long sufferer from this affliction I am convinced that the main causes of failure are (1) too weak a local anaesthetic, (2) too elaborate an operation. For this reason I recommend a 10% solution of cocaine as the anaesthetic and a plain curved surgical needle, bayonet edged, as the only surgical instrument necessary. The strong solution of cocaine rapidly brings the movements of the filaria under control, and the extraction of the worm is effected by simply passing the sharp point of the needle through the conjunctiva and under a coil of the worm, which is then rapidly extracted by withdrawing the needle and worm through the incision made by the sharp edges of the needle. Damage to the conjunctiva is negligible, and the only complication is a painful eye some hours later due to the effects of the cocaine. I might mention that at my own request this method has been employed on myself on five occasions without a failure. One of these extractions was carried out by an inexperienced layman, who, without the help of an anaesthetic, proved very skilful. More elaborate methods have been employed on me, but none has succeeded.

Treatment of Cataract.—Dr. RONALD KERR (West Hampstead, N.W.) writes: The answer to the question on the treatment of cataract (June 21, p. 911) is far too sweeping in its condemnation of medical treatment. Mature cataracts, of course, need operation, but in the early stages the lens changes are reversible, and if the physician can spend time on the case and the patient will co-operate it is usually possible to stay the progress of early senile cataracts and to effect some improvement in some of them. Senile cataract, being a degenerative change, has as its cause any factors leading to lowered health and premature senility. As there are thus many possible causes, it is hardly to be expected that there should be *a* treatment; but this does not mean that any treatment is necessarily futile. One must treat the patient rather than the cataract, and regulation of diet to include adequate quantities of mineral salts, vitamins, and water to drink, avoidance of excessive common salt, reduction of weight where required, hormone therapy, and elimination of foci of infection may all be needed in treatment. If there is also present some other condition, such as rheumatism, which indicates an endogenous infection, treatment should include injections of autogenous vaccines in small doses. (Indiscreetly large doses of such vaccines can cause rapid progress of the cataract.) Treatment can never become purely routine, and it would be interesting to know whether the person who answered the question (who is presumably a surgeon) has any personal experience of determined medical treatment of these early cases.

Urinary Incontinence.—Mr. H. P. WINSBURY-WHITE, F.R.C.S. (London, W.) writes: I am interested in this question and answer concerning incontinence of urine of four years' duration in a man aged 34 (July 5, p. 41). I have examined a considerable number of cases where the onset of the complaint has occurred in adult life. This experience enables me to say that endoscopy which omits urethroscopy is an inadequate examination. My reason for this assertion is that I have found a lesion in the posterior or membranous urethra is commonly present; moreover the way in which the incontinence usually yields to proper treatment of the lesion makes it quite clear how dependent the symptom is upon the urethral pathology.

Corrections

Dr. Ethel A. Orchard writes to point out that in our report of the annual dinner of the Association of Surgeons of Great Britain and Ireland (July 12, p. 79) the Commonwealth Travelling Professorship in Medicine (founded by Mr. Arthur Sims) was incorrectly described as the Commonwealth Travelling Fellowship.

In the bibliography to Dr. J. G. Salter's letter (July 19, p. 108) the reference to Rauch, J. H., and Saayman, L. R., should be *S. Afr. med. J.*, **12**, 885.

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